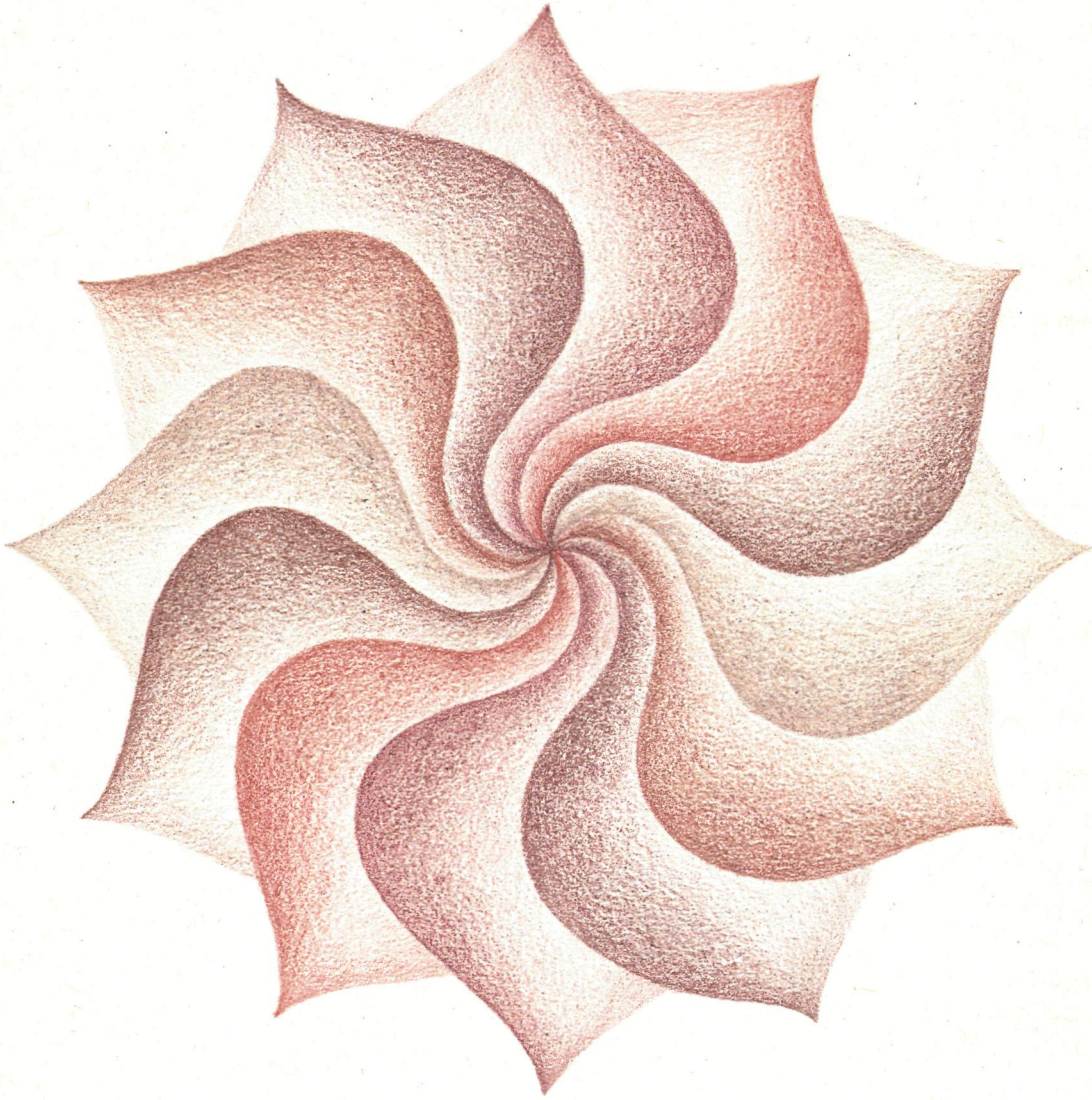
Chronic diseases in general practice

Comorbidity and quality of care



François Schellevis

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Comorbidity and quality of care

Chronische ziekten in de huisartspraktijk

Comorbiditeit en kwaliteit van zorg

Een wetenschappelijke proeve
op het gebied van de Medische Wetenschappen.

Proefschrift
ter verkrijging van de graad van doctor
aan de Katholieke Universiteit Nijmegen,
volgens besluit van het College van Decanen
in het openbaar te verdedigen op
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door

François Georges Schellevis

geboren op 9 februari 1953
te Biezelinge

Promotores: Prof. Dr. C. van Weel
Prof. Dr. J.Th.M. van Eijk (Vrije Universiteit Amsterdam)

Co-promotor: Dr. E.H. van de Lisdonk

The following institutions participated in the study reported in this thesis:
- Department of General Practice and Social Medicine, University of Nijmegen;
- Netherlands Institute of Primary Health Care (NIVEL), Utrecht;
- Department of General Practice and Nursing Home Medicine / Institute for Research in Extramural Medicine, Vrije Universiteit Amsterdam.

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Preface

For everything there is a season,
and a time for every matter under heaven:
... a time to keep silence,
and a time to speak ...

Ecclesiastes 3:1,7b

Time has always been an important and intriguing phenomenon to me. Time is a major diagnostic and therapeutic tool in general practice where most health problems are self-limiting. Confidentiality and trust in a patient-doctor relationship needs time to develop. Time is inevitable in building up families and generations, the highly important milieu for general practitioners. For continuity of care, especially relevant in chronic diseases, time is conditional. Chronic diseases as subject of my thesis fit very well in this field of interest.

This thesis is based on a project with research and developmental aspects which started in December 1986 - time flies. The research questions evolved during the course of the project. While initially measurements of prevalences and validity of diagnoses had been planned, during the project comorbidity of chronic diseases emerged as a theme of increasing importance. Moreover, the extensive phase of analytic and reporting activities, starting in June 1991, contributed, in my view, to a more balanced product. This thesis is a result of a process rather than of an activity, a snapshot in an ongoing way of thinking rather than a definite outcome.

May this thesis contribute to a further improvement of the quality of general practitioners' work in their care of patients with chronic diseases.

Contents

1. Introduction

... The inevitability of the growth of the elderly population is certain to have a profound influence on the health care industry in the coming decades ... •

1.1. Demographical and epidemiological developments

The human species has entered a new era in its demographic evolution: population aging. The proportion of the population surviving into older ages is at a level unprecedented in human history [1]. Consequently, the attention of health care providers and medical investigators shifted during the last decades from the length to the quality of life, especially in old age. This has been expressed in the well-chosen phrase "adding life to years, not years to life" [2]. From the epidemiological point of view The Netherlands, like most countries in Western Europe and Northern America, nowadays are in the fourth phase of the epidemiological transition [3] or the "age of delayed degenerative diseases" [4]: the lengthening of human life is reaching a limit, and - due to more accurate diagnostic and therapeutic tools - degenerative and chronic diseases are detected earlier in life. Lengthening of this 'lead time' and more sophisticated medical care lead to a longer lifetime with disease, which is referred to as decompression or expansion of morbidity.

Health measures, aimed at compression of morbidity [5,6], include primary prevention of chronic diseases by the elimination of causal factors. Primary prevention is the field of biomedical sciences, epidemiology, and public health. Secondary prevention is the early detection and effective initial treatment of diseases. Secondary prevention has a positive influence on the course of a chronic disease, even at older ages [2,7]. Tertiary prevention includes health care for patients with established chronic diseases and aims at compression of disabling lifetime. The impact of tertiary prevention on quality of life has only recently been recognized as a field of interest [8].

Growing older implies a higher risk at chronic diseases and consequently a higher risk at comorbidity of chronic diseases as incidence rates of the most common chronic diseases are age-dependent or aging-related [9]. The expected increase of the proportion of people of 65 and over from 12.5% in 1988 to more than 21% in the year 2050 [10], will considerably change the morbidity pattern of the practice population of general practitioners (GPs) [11], especially with regard to chronic diseases.

• *Olshansky SJ, Ault AB. The fourth stage of the epidemiologic transition: the age of delayed degenerative diseases. Milbank Q 1986;64:355-391.*

1.2. Chronic diseases in general practice

Studies on chronic diseases in general practice may increase our insight into the management of chronic diseases in general practice, and anticipate these future changes. Chronic diseases in the general population have recently been studied in view of public health policy [12]. In other recent studies incidences and prevalences of chronic diseases in general practice and aspects of the care for the elderly have been reported [13,14]. An earlier study in The Netherlands focused on comorbidity of newly diagnosed diseases [15]. In the United Kingdom chronic diseases in general practice received attention from the educational point of view [16,17].

1.3. Objective of this study

The objective of this study was to gain insight into the prevalence of chronic diseases in general practice and into the care of patients with chronic diseases provided by GPs. This global objective was pursued in detail guided by the following questions:

a. How can comorbidity be defined?
b. What is the validity of diagnoses of chronic diseases in general practice?
c. What is the prevalence of comorbidity of chronic diseases?
d. What is the influence of comorbidity of chronic diseases on GP consultation rates and on the incidences of intercurrent diseases?
e. Does the actual care of GPs during the follow-up of patients with chronic diseases become more in agreement with consensus guidelines for optimal care in course of time?
f. What is the effect of the implementation of guidelines for follow-up care on the disease status of patients with chronic diseases in general practice?

The study reported in this thesis is a part of the Dutch National Survey of General Practice, which is aimed at gaining insight into the patterns of diseases presented in general practice and into the care provided by GPs [18]. This part of the survey focuses on chronic diseases with special attention to comorbidity and quality of care.

Comorbidity of chronic diseases, the existence of more than one chronic disease in one patient, has not received much attention, until recently. Comorbidity is, however, a reality of the daily practice of GPs who have to deal with all diseases of a patient.

The second major theme, the care for patients with chronic diseases, is studied from the viewpoint of the quality of care, which is one of the concepts in the research of health care of patients with chronic diseases [19]. Quality of GP care has been given increasing attention in The Netherlands, especially trough the development of 'standards' initiated by the Dutch College of General Practitioners [20]. However, the development of measures for the quality of care, has received much less attention so far.

1.4. Chronic diseases

Defining chronic diseases is not a simple matter. A diagnostic definition, such as the definition of the U.S. Commission on Chronic Illness [21], is widely used but this definition comprises a broad range of health problems. Limitation to those chronic diseases that are listed in the Health Interview Survey [22] is a pragmatic approach, but is more appropriate for studies of the general population. The use of criteria for chronicity is another approach, some of which have been applied in recent studies [12,13,23,24]. The following criteria are commonly used:

a. a minimum duration of the disease, varying from 3 to 6 months, or the frequency of recurrence of the disease;
b. the severity of the disease, often determined by the degree of impairment or disability;
c. the demand for (professional) health care.

During the preparation of our study we decided to determine the choice of chronic diseases by the following criteria:

1. the nature of the disease (generally accepted as chronic);
2. its relatively high prevalence in the general practice population;
3. the fact that GPs usually carry the first responsibility for the care of these patients.

This third criterion excluded cancer, which is mainly managed by specialists, although it is recognized that patients with malignant neoplasms often receive extensive care from GPs too. Also excluded were mild chronic psychiatric disorders with a high prevalence in the general practice population, that are responsible for a substantial part of the GP workload. Psychiatric disorders are difficult to define, and the type of delivered care depends largely on the personal preference of patient and doctor, and on the skills of the GP. Therefore, prevalence and management of psychiatric disorders can better be studied separately. Chronic neurological conditions, such as Parkinson's disease and multiple sclerosis, have also been left aside. The prevalence of these diseases is relatively low, and not the GP but the neurologist is mostly the first responsible for the care of these patients.

These considerations led to the choice of the following five chronic somatic diseases for this study:

- hypertension (strictly speaking not a disease but a risk factor);
- chronic ischemic heart disease (angina pectoris, previous myocardial infarction);
- diabetes mellitus;
- chronic respiratory disease (asthma, chronic bronchitis, emphysema);
- osteoarthritis of hip and/or knee.

1.5. Quality of care

The concept of quality, a frequently used and misused term, is difficult to define [25]. For use in the health care field, the concept of quality is often made operational by listing the characteristics of care which are considered to be related to its quality, e.g. effectiveness of medical procedures, availability of care, respectful attitude of professional caregivers [26]. The cyclic process of quality management comprises three

elements: quality measures (e.g. guidelines), quality assessment, and quality improvement [27].

The formulation and implementation of guidelines that reflect qualitatively good care is essential in assessing and improving quality of care [28]. The availability of such guidelines makes it possible to compare actually delivered care (performance) with optimal care. Since 1989 standards for optimal care are being developed by the Dutch College of General Practitioners. The problems encountered in developing and in implementing guidelines for good care have recently been surveyed [29,30].

In assessing the quality of care three aspects of care are usually considered: structure, process, and outcome [31]. The theoretically ideal process of quality assessment and quality improvement meets many obstacles on its way to realization. Recently it was concluded that a systematic evaluation of the impact and effect of guidelines on the quality of care in general practice is still lacking [29]. In this study the effect of the formulation of guidelines and their implementation within a peer review process on the process and outcome of care is evaluated. The method of peer review, which was chosen for this study, is one of the possible strategies in assessing and improving quality of care [27]. This method was considered feasible within the framework of this study in view of the number of participating GPs and in view of the available experience with this method [32,33].

1.6. General practice in The Netherlands

The task of the general practitioner as adopted by the Dutch College of General Practitioners is to deliver continuous, integral, and personal care to individual patients and their families [34]. In The Netherlands all non-institutionalized inhabitants are registered in a general practice. Generally, members of one family have the same GP. Continuity of care over generations and over time is highly important. The mean practice list size is about 2300 persons. About half of the GPs work individually, one third in a practice with two GPs, and the others in a group practice or health centre. In most practices one or more practice assistants are present. Their tasks vary from mere administrative work to performance of medical procedures under supervision, depending on their skills and the willingness of the GP. There are daily consultation hours at the office. Home visits are made upon request.

In regional groups GPs organize their educational activities, and the evening and weekend services. There is no free access to specialized care: referrals are to be made by the GP. GPs can use laboratory facilities, and imaging and other diagnostic services without having to refer patients to a specialist.

General practitioners in The Netherlands are in a favourable position to deliver continuous care in every respect. The setting of general practice is well suited for the management of comorbidity of chronic diseases and the optimalization of the care of these patients. GPs can play a leading part in assuring the quality of life of patients with chronic diseases and comorbidity. These will be important challenges for the near future.

1.7. Outline of the thesis

Chapter 2 contains a systematic analysis of the literature on comorbidity. This review especially focuses on the definition of comorbidity and on methodological aspects. In chapter 3 a study on the validity of diagnoses of chronic diseases is described. Validity is measured by the agreement of diagnostic procedures with diagnostic inclusion criteria. A prevalence study on the extent of comorbidity of five common chronic diseases in general practice is reported in chapter 4. Chapter 5 describes the influence of comorbidity of chronic diseases on the number of GP consultations and on the extent of intercurrent morbidity. The chapters 6 and 7 report on the effects of formulation and implementation of guidelines for optimal follow-up care of patients with chronic diseases. In chapter 6 the effect on GP performance is described, chapter 7 presents the effect on outcome measures in patients with chronic diseases. The thesis finishes with chapter 8 in which the research questions are answered, and the study is discussed in general. A summary in different languages concludes this thesis.

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2. Comorbidity - definitions and methodological aspects

... How can medicine, which is commonly supposed to be a science, be so different in countries whose peoples are so similar genetically? ...[*]

Abstract - *In studying the literature on comorbidity very diverse definitions and applications of this concept were found. This led to a systematic literature search to make an inventory of definitions of comorbidity, of the diseases that are considered in studies of comorbidity, and of the methodological aspects of comorbidity. A systematic search through MedLine since 1985 yielded 70 publications. Reviewing these publications showed that in 33 publications an explicit definition of comorbidity was mentioned. Definitions depended upon the type of relation between diseases. Three categories were distinguished: co-existence of diseases without any reference category, presence of other diseases than an index disease, and a relationship (association, correlation) between diseases. A wide variety of diseases was considered in the context of comorbidity. Most publications agreed upon the chronic nature of the comorbid diseases (diabetes, cancer, heart diseases). Most publications reported cohort or cross-sectional studies. In the reviewed publications comorbidity was most frequently used as an independent variable in the study (28 publications), less frequently as a confounding or modifying variable (23 publications). Measures of comorbidity included multiple variables indicating the presence or absence of specific diseases separately, the number or sum of diseases, one variable (indicating the presence or absence of any comorbid disease), and comorbidity indexes. Five different indexes were traced. Mortality or survival was the main outcome variable in 32 publications, in thirteen publications comorbidity was the main outcome variable. A classification of comorbidity is proposed, based on the relationship between diseases. It is concluded that for a better understanding of the role of comorbidity there is a need for an agreed definition, for explicit mentioning of the diseases considered and for standardization of measures of comorbidity.*

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[*] *Payer L. Medicine and culture. New York: Penguin Books, 1988.*

Schellevis FG, Velden J vd, Eijk JThM v, Lisdonk EH vd, Weel C v. Comorbidity - definitions and methodological aspects [Submitted].

2.1. Introduction

In recent years comorbidity has been recognized as an issue of interest in clinical epidemiological literature. For practising physicians the existence of multiple diseases in a single patient is evident, especially for disciplines of geriatrics, of nursing home medicine, and of general practice where the focus is not on the management of one specific disease or disorder. In medical research comorbidity is often dealt with as a possible cause of heterogeneity: patients with comorbidity are therefore often excluded from clinical trials. Several authors emphasize the limited external validity of the results of trials in which patients with specific characteristics as comorbidity are excluded [1-4].

In the literature on comorbidity many different ways of defining and handling the concept of comorbidity were found. This led to a systematic search in literature with the following questions:

* How is comorbidity defined and how can these definitions be classified?
* Which diseases are considered in studying comorbidity?
* How is comorbidity methodologically handled?

The aim of this report is to clarify the differences in handling the phenomenon of comorbidity in order to contribute to greater uniformity. The use of standard definitions and uniform measures for comorbidity may lead to better comparability of study results and consequently to a better understanding of the role of comorbidity.

2.2. Methods

Selection procedure

The material for this literature study was collected by a systematic search in MedLine (CD-ROM, Silver Platter), using 'comorbidity' as the only search criterium (present as an index key word, or appearing in the title or in the abstract) in publications between 1985 and 1991. This resulted in a number of 379 titles (Table 2.1).

Table 2.1. Number of references resulting from MedLine search with key word comorbidity per publication year

Year of publication	Number of references (abs)
1985	1
1986	12
1987	18
1988	40
1989	77
1990	97
1991	134
Total	379

On this material a four-step selection procedure was carried out (Figure 2.1).

Step 1

Considering only the title of the publication and bibliographical specifications the next exclusion criteria were applied:

a. language: other than English or Dutch;
b. type of publication: case study, letter to the editor;
c. major emphasis on psychiatric morbidity (in the psychiatric literature the term comorbidity is often used for the combination of a major mental illness with substance abuse and addiction disorders).

On the basis of these criteria 232 titles were excluded.

Step 2

Of the remaining 147 titles the abstract, generated by MedLine, was studied. Excluded were publications meeting one of the following criteria (in parentheses the number of publications meeting this criterium):

a. comorbidity in relation to diseases of dental origin (N=3);
b. comorbidity in relation to exogenous factors as exposure to physical agents (N=6);
c. comorbidity in relation to remuneration systems of health care (N=14);
d. editorials and abstracts indicating a publication with emphasis on education or reflection (N=27);
e. abstracts indicating that comorbidity is a minor point in the study (comorbidity is an exclusion criterium, comorbidity is only mentioned in the discussion section as a hypothetical explanatory variable, the term comorbidity does not appear in the abstract) (N=37).

The main reason for excluding publications on dental diseases, on financial topics, and on exogenous factors was the primary interest in the aspect of medical care. In this way 87 publications were excluded.

Step 3

The remaining 60 publications were carefully studied. The publications were categorized on the basis of the type of population in which the study took place (in parentheses the number of publications):

- general population (N=9) [5-13];
- outpatient clinic population (N=9) [14-22];
- patients during and after hospitalization (N=33) [23-55];
- patients treated in dialysis centres (N=8) [56-63];
- autopsy studies (N=1) [64].

The last two categories of studies were excluded in this review.

Step 4

Any reference listed in the remaining 51 publications that seemed to be relevant in the context of this literature study, was studied and tested by the criteria mentioned in the first two selection steps. References to sources other than journal publications (e.g. reports, books) were not traced. This yielded another 16 eligible publications, three studies in the general population [65-67], three in a setting of an outpatient clinic [68-70], and 10 studies in hospitalized patients [71-80]. Screening of the titles of the

references listed in these 16 additional publications did not produce new sources. On the contrary, the circle of references seemed to close. Finally, three publications published in 1991 were added from the personal archive of the first author [81-83], one of a study in the general population, and two in a general practice setting. This resulted in a total of 70 publications that have been reviewed.

Figure 2.1. Selection of publications for a review on comorbidity

	Procedure		Number of publications
MedLine search 1985-1991: publications with 'comorbidity' as key word, or appearing in title or abstract			379
1	Excluded on the basis of: language, type of publication, or psychiatric morbidity		- 232
		Remaining	147
2	Excluded on the basis of: subject (dental diseases, exogenous factors, financial issues), editorial or educational paper, or comorbidity as minor point		- 87
		Remaining	60
3	Excluded on the basis of setting (dialysis centre, autopsy)		- 9
		Remaining	51
4	Additional publications		
	a. from references of included publications		16
	b. from personal archive		+ 3
	Number of selected publications		70

Reviewing procedure

All publications were screened for *definitions* of comorbidity. Only definitions explicitly mentioned in the publication are considered. It was decided not to use implicit definitions, formulated on the basis of the context in which the term comorbidity is used, as this may introduce observer bias.

The *diseases* or disease categories that were included under the term comorbidity in each publication, and the sources from which information about diseases was abstracted

were listed. In the publications studied a wide range of disease classifications, from global to detailed, was found. The diagnostic terms were left intact, except that obvious synonyms like 'pulmonary' and 'respiratory' were grouped together. Different types of sources of information on diseases are distinguished: self-report (written or by oral interview), medical records (including hospital charts, hospital discharge forms, clinical records, death certificates), and medical examinations, specially carried out for the study. Special attention is given to information in the publications about the application of diagnostic criteria in defining comorbid diseases.

The *methodological aspects* the publications were screened for are the design of the study, the place or function of comorbidity in the study design and the way comorbidity is transformed to one or more measures for analysis. The place of comorbidity in the studies is categorized in four categories: outcome variable, independent variable, confounding/modifying variable, and a rest category. Measures of comorbidity used as analysis variable are classified as follows:

a. comorbidity present or absent (one dichotomous variable);
b. number of diseases / sum of comorbid diseases (one continuous variable);
c. presence or absence of specific diseases or disease categories separately (multiple dichotomous variables);
e. index of comorbidity, indicating diseases weighted for, mostly, their severity.

The term comorbidity refers to a co-existing ailment, additional to a particular 'index' disease [84]. As the operationalisation of comorbidity is strongly related to the index disease, which indicates the main characteristic of the study population or the main independent variable in the study, index diseases were taken into account in studying the methodological aspects.

2.3. Results

Definition of comorbidity

In 33 of the 70 publications an explicit definition of comorbidity was mentioned (in one publication two subclasses of comorbidity were defined). In most definitions the relationship between diseases is the central item. Therefore, it is logical to classify these definitions on the basis of the type of relationship between diseases (Table 2.2) (in parentheses the number of publications):

A. co-existence of diseases without mentioning any reference category (N=13);
B. presence of diseases other than the index disease (N=12);
C. relationship (association, correlation) between two diseases (N=9).

Definitions in the classes A and B suggest that a random co-existence of diseases is assumed, whereas definitions in the third class are based on a hypothesis of a certain relationship. Definitions in class B differ from those in class A in the explicit mentioning of an index disease. The definitions in class C give more detail about the kind of relationship between the studied diseases.

Table 2.2. Definitions of comorbidity, explicitly mentioned in 33 publications

Co-existence of diseases without any reference category
- 'all chronic conditions they had' [5]
- 'presence of multiple health conditions' [6]
- 'co-existence of chronic conditions' [7]
- 'co-existing diseases at the time of hospitalization' [32]
- 'co-existing diseases' [33,42]
- 'secondary diagnoses at the hospital discharge' [43]
- 'secondary diagnoses listed at discharge that represented chronic disease that would be unlikely to occur as in-hospital complication' [52]
- 'having several chronic conditions simultaneously' [66]
- 'co-existence of multiple diseases and conditions' [67]
- 'co-existence of chronic conditions or impairments in the same person' [81]
- 'concurrent (pathological) conditions and disorders' [82]
- 'diseases occurring together within a 12 month period' [83]

Presence of diseases other than an index disease
- 'presence of one or more of the other 36 health conditions [than the index condition]' [9]
- 'other medical conditions that were not specifically identified as possible causes of [the index disease]' [10]
- '[index disease] co-existing with other chronic diseases' [11]
- 'occurrence of [the index disease] in conjunction with other chronic conditions' [12]
- 'other health problems present which could, by themselves or interacting with [the index disease] cause [dependent variable]' [13]
- 'occurrence of [disease A] in patients with [the index disease]' [15]
- 'medical problems or functional limitations other than those due to [the index disease]' [17]
- 'other sources of morbidity that may also influence [the dependent variable]' [19]
- 'conditions, other than the patients' [index disease] that may have had an impact on [the outcome variable]' [28]
- 'presence of other health conditions than [the index disease]' [69]
- 'clinical conditions other than [the index disease] that might have been expected to impair [the outcome variable]' [76]
- 'ailments that co-exist with a "main" disease' [80]

Relationship (association, correlation) between diseases
- 'relationship between [disease X] and [the index disease]' [8]
- 'association between [index disease] and [disease X]' [20,21,65]
- 'correlation between [disease X] and [disease Y]' [22]
- 'symptomatic associated diseases at the onset of [the index disease]' [26]
- 'any associated disease at the time of the [index disease]' [49]
- 'complicating conditions' [74]
- 'associated conditions [at the same site as the index disease] that might have been responsible for the local symptoms attributed to the [index disease]' [76]

Comorbid diseases

In 17 of the 70 publications comorbidity was not specified in terms of diagnoses [6,12,28,30,32-36,53,55,70,72-74,77,78]. In 14 other publications [7,9,13,19,23,24,29,37,66, 68,75,79,81,83] the reader, looking for diseases, was referred to references on existing instruments as the Supplement on Aging of the National Health Interview Survey [7, 13,66,81], or indexes as the Comorbidity Damage Index [23,24] and the Charlson Index [29,37]. Only the diseases that were mentioned explicitly were considered. Two

publications made no restrictions in the diseases that were included under the term comorbidity [79,83]. Table 2.3 lists the diseases that were most frequently mentioned. The chronic nature of these diseases is evident. Although the index diseases in the selected publications differed widely (see Appendix), the authors apparently agreed upon the nature of relevant comorbidity in the different studies. It is striking that also risk factors as hypertension, smoking, alcohol and drug use were labelled as comorbid conditions.

Table 2.3. Diseases or disease categories most frequently mentioned in studying comorbidity (number of publications in which the disease was mentioned in parentheses)

Disease or disease category	Reference #
Diabetes mellitus (N=28)	5,7,8,16,19,21,23,24,26, 29,37,38,39,41,42,43,44,45, 46,47,48,49,50,66,67,69,71,81
Hypertension/ high blood pressure (N=28)	7,14,16,19,21,23,24,27, 29,31,37,38,39,41,42,43,44, 46,47,49,50,65,66,67,69,71,80,81
Cancer, incl. specifications (N=23)	5,7,11,19,20,23,24,27, 29,31,37,42,46,48,49,52,54, 66,67,69,76,80,81
Ischemic heart disease/ angina/myocardial infarction (N=16)	21,23,24,27,29,37,38,39, 41,42,43,48,49,65,66,71
Pulmonary/respiratory/ lung disease (N=12)	8,19,23,24,29,37, 47,48,69,75,80,81
Heart disease (N=12)	5,7,16,42,46,47, 50,52,54,69,80,81
Peripheral vascular disease (N=11)	23,24,26,29,37,38, 39,47,48,52,80
Cerebrovascular disease/ stroke (N=10)	7,16,27,29,37,38,48,66,67,81
Kidney/renal disease (N=10)	5,19,23,24,42,48,54,69,75,80
Congestive heart failure (N=9)	23,24,27,29,37,38,41,48,52

In 11 publications the source of data on diseases was not mentioned [14,16,27,28,32-34, 45,46,49,77] or not relevant (written cases [17] or review [54]). Diseases based on self-report were used in 14 publications [5-7,9,12,13,19,44,66-70,81]. Three publications reported a special examination [15,65,82] as the basis for determining comorbid

diseases. In the other publications comorbidity data originated from medical records solely, or in combination with self-report. In six publications information was given on the applicated diagnostic criteria in diagnosing comorbid diseases [15,22,36,41,65,80].

Design

Most publications in which comorbidity plays a substantial role were cohort studies or include a cross-sectional design (Table 2.4). Eight publications regarded the validation of an index of comorbidity or of an index in which comorbidity is included. None of the 70 publications reported a study with a design allowing conclusions about causal relations between independent and dependent variables.

Place of comorbidity in the design

In 13 publications comorbidity was the main outcome variable (Table 2.4 and Appendix). Comorbidity appeared most frequently as an independent variable, less frequently as a variable that confounds or modifies the relation between independent and dependent variable.

Table 2.4. Summary of methodological aspects of 70 publications on comorbidity (for full overview see appendix)

	Number of publications
Design [1]	
Cohort study	33
Cross-sectional study	20
Validation study	8
Case control study	4
Longitudinal study	3
Reliability study	1
'Delphi'-process	1
Review	1
[1] one publication included 2 designs	
Place or function of comorbidity in the design [2]	
Independent variable	28
Confounding / Modifying variable	23
Outcome variable	13
Variable to be validated	7
Variable to be compared	1

[2] two publications included more than one function of comorbidity in the study

Table 2.4. Summary of methodological aspects of 70 publications on comorbidity (for full overview see appendix) - continued

	Number of publications
Measure of comorbidity [3]	
Existence of specific diseases	33
Number (sum) of diseases	18
Existence of comorbidity	13
Index of comorbidity	13
[3] seven publications used two types of measures	
Main outcome variable [4]	
Mortality or survival	32
Demand/use of health services, incl. type of treatment	13
Comorbidity	13
Disability/functional health	11
Incident morbidity/complications	10
Other	14
[4] a total of 93 different outcome variables were identified	

The index diseases cover a broad variety of diseases or conditions (see Appendix). Apparently, comorbidity was a variable of interest in studies on (rheumatoid) arthritis (N=11 publications), cardiovascular diseases (N=10), cancer (N=6), and diabetes mellitus (five publications).

Measures of comorbidity

There were major differences in the way comorbidity was handled in the analysis in the 70 reviewed publications (Table 2.4). In almost half of the publications comorbidity was included in the analysis as multiple variables, indicating the presence or absence of specific diseases or disease categories separately. The number (sum) of comorbid diseases is a measure that was mentioned in 18 publications. The use of one variable indicating the presence or absence of any comorbid disease is less popular. This is also true for the use of an index. A total of five different indexes, which are primarily focused on comorbidity, were mentioned. The earliest index mentioned in the selected publications classified comorbid diseases in grades of severity [80]. This index was the basis for a second index, generally referred to as the "Charlson Index", including the extent of comorbidity weighted for severity [29]. Greenfield et al. developed an index for comorbidity weighted for the stage of disease, complications, and functional status [28]. Two publications mentioned an index which was apparently specifically developed for that study [17, 73].

Mortality or survival is the outcome variable most studied in publications regarding comorbidity.

2.4. Discussion

A systematic search in MedLine by means of a key word that is a non-Index Medicus term carries the risk of being incomplete. Another reason for possible 'under-selection' is the assignment of key words by the authors. It can be assumed that comorbidity is used in many more studies. By selecting publications on the basis of the term comorbidity as key word, bias due to the authors by not assigning comorbidity as key word or by not mentioning it in the abstract cannot be excluded. To fill this gap, all references of the selected publications were systematically screened, resulting in the additional 16 eligible publications. Several authors are represented more than once in our selection; screening bibliographical indexes using these authors' names could perhaps reveal more publications.

Definition of comorbidity

In contrast with the term multiple diseases or multiple pathology, the term comorbidity suggests the existence of an index disease as starting point, and that there are other diseases at the same time in the same patient [84]. The relation between the index disease and the comorbid disease(s) is obviously the basis for the definitions of comorbidity in the reviewed publications.

A previously proposed classification of comorbidity [84] was based upon the impact of comorbidity in different clinical situations, e.g. comorbidity that hinders the diagnostic process, or comorbidity influencing the prognosis of an established disease.

The following classification that is being developed, is based upon the type of the assumed relationship between diseases. It consists of four categories:

a. *concurrent comorbidity*: the co-existence of diseases in the same person without any satisfying explanation, e.g. cardiovascular disease and osteoarthritis;
b. *cluster comorbidity*: the distribution of diseases in a population shows concentrations in subgroups that differ significantly from the distribution by chance, e.g. multiple sclerosis and epilepsy [15];
c. *causal comorbidity*: interrelation of diseases based on a proven common pathophysiological cause, e.g. ischemic heart disease and peripheral arterial disease;
d. disease-specific *complicating comorbidity*: the existence of one disease is obligatory for the occurrence of another disease, e.g. diabetes mellitus and diabetic retinopathy.

This classification structures the relationship between an index disease and one or more other diseases.

Whether and which types of comorbidity are relevant in a certain study depends mostly on the questions to be answered. Concurrent comorbidity is potentially relevant for clinical practice, e.g. when the presence of one disease is a contra-indication for the pharmacological treatment of a second disease. Cluster comorbidity is an interesting phenomenon for clinical researchers and can turn out to be important in describing a new syndrome [85]. Causal comorbidity and complicating comorbidity are clinically relevant for the management of diseases and their complications, for surveillance, and for screening and prevention.

Comorbid diseases

A substantial number of the publications agree upon the diseases that constitute comorbidity: mostly chronic diseases with a high prevalence. Apparently, acute medical conditions are considered to be less relevant co-morbid diseases. The inclusion of risk factors (e.g. smoking, alcohol abuse) as comorbid diseases is dubious. When they are separately considered in a study, it is not necessary to label them as comorbid conditions. When they are included in a variable at a more aggregated level as an index, it is questionable whether this information is comparable with other variables constituting that index.

In only a small minority of the publications the application of diagnostic criteria in confirming the existence of comorbid diseases was explicitly mentioned. This raises questions about the validity of morbidity data that are used in the other publications, especially when the information originates from self-report [86-88].

Methodological aspects

The question of which diseases should be considered in terms of comorbidity depends, of course, on the function of the variable 'comorbidity' in the study (independent variable, dependent variable or confounder/modifier). In general, it is recommended to specify beforehand in detail which diseases or conditions are relevant within the context of the study. Global measures, such as the number (sum) of diseases or conditions, seem to be a relevant predictor (see, for example [81]). However, when more detailed measures are used, results can more easily be interpreted and are probably more relevant in practice.

2.5. Conclusions

Comorbidity has been given increasing attention in literature and research. It seems, however, that every author uses his own definition of comorbidity and handles comorbidity by his own method. Explicit mentioning of definition, diseases considered, and of analytic methodology in the management of comorbidity in research publications would be an important first step on the road towards standardization. The usefulness of a distinction between 'causal comorbidity' and 'comorbidity by chance' needs further study.

This review is an exploration in the complex world of comorbidity. It is an attempt to introduce a systematical approach that hopefully will stimulate further creative conceptual and research work in this field.

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3. Validity of diagnoses of chronic diseases in general practice

The application of diagnostic criteria

... Diagnostic labels are a kind of clinical shorthand; they are based on agreement and on generally accepted defining criteria; they have no intrinsic value...[•]

Abstract - *Certainty of a diagnosis is not only important for the patient but also for morbidity studies. In the absence of a gold standard, agreement with diagnostic criteria is often the best approach in measuring the certainty of a diagnosis. The agreement with diagnostic criteria has been studied for 5 chronic diseases (hypertension, chronic ischemic heart disease, diabetes mellitus, chronic nonspecific lung disease and osteoarthritis) in 7 general practices with a total practice population of 23,534 persons. Agreement with diagnostic criteria is operationalized into 3 categories. For each chronic disease a diagnostic quality measure per general practitioner is computed. Retrospective data have been collected in the practices on 2295 diseases in 1989 patients. Two-thirds of the diagnoses were made in general practice. The agreement with the diagnostic criteria for the cases diagnosed in general practice is high, ranging from 96% true positive cases in diabetes mellitus to 58% in chronic nonspecific lung disease. The highest rate of false positive cases is 4%. On the level of general practitioners diagnostic qualities vary from 62 to 96% true positive cases for the different diseases. The variation in diagnostic quality between general practitioners is substantial. The prevalence rates for the 5 chronic diseases are lower after adjustment by only including true positive cases. Diagnoses of the 5 chronic diseases recorded in general practice are generally valid with low numbers of false positive cases.*

• *Sluiter HJ, Koëter GH, Monchy JGR de, Postma DS, Vries K de, Orie NGM. The Dutch hypothesis (chronic non-specific lung disease) revisited. Eur Respir J 1991;4:479-489.*

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3.1. Introduction

The management of chronic diseases is considered to be the "very stuff of general practice" [1]. The diagnostic process and long-term care are two major clinical aspects of managing chronic diseases in general practice.

An increasing number of publications deals with various aspects of the long-term care of patients with chronic diseases: the organization of care and the management of chronic diseases [2], standards in view of the quality of care [3], and compliance with therapy and follow-up controls [4]. Much less attention has been given to the process of diagnosing a chronic disease in general practice. Yet the diagnosis of a chronic disease is of great importance: it labels the patient, often for his lifetime, and often has implications for daily life. Those suffering from a chronic disease are at risk of complex or serious illness, and of potentially harmful medical interventions. Therefore, the certainty of the diagnosis of a chronic disease is of crucial importance: false-positive and false-negative diagnoses may have unacceptable consequences for the patient.

Apart from the importance of accurate diagnoses for the patient, certainty of the diagnosis is important for epidemiological research. This is especially the case in countries like the U.K. and The Netherlands where all non-institutionalized persons are registered in a general practice, which allows a valid estimation of the epidemiological denominator. Estimations of morbidity rates often rest upon population surveys with self-report about diseases. In measuring the concurrent validity of these data a comparison is often made with morbidity data from medical sources on the assumption that the latter data have a higher validity [5-7].

The aim of this study was to establish the validity of the diagnoses of chronic diseases on medical records in general practice.

Unfortunately, there is no absolute certainty or "gold standard" for diagnoses, except for some areas where diagnostic criteria are linked to underlying pathologic confirmation. Therefore, agreement with a set of diagnostic criteria is usually the best approach. Diagnostic criteria, often determined by international expert fora, reflect the actual common consensus on the nature and outcome of diagnostic procedures determining the diagnosis. The International Classification of Health Problems in Primary Care (ICHPPC) [8] lists diagnostic criteria to be used in general practice.

The application of such criteria in diagnosing chronic diseases in general practice has not been widely studied. A pilot study performed in Maastricht (The Netherlands) to evaluate the feasibility of application of criteria in daily work in general practice provided encouraging results [9].

We have compared information on applied diagnostic procedures by general practitioners in diagnosing patients with hypertension, chronic ischemic heart disease, diabetes mellitus, chronic nonspecific lung disease, and osteoarthritis of hip and/or knee with the diagnostic criteria of the ICHPPC-2. We also describe the effects of only including true positive cases on the prevalence rates of these chronic diseases.

3.2. Methods

Practices and population

From 103 practices that took part in the "Dutch National survey of morbidity and interventions in general practice" [10] (a non-proportional stratified random sample of all general practitioners in the Netherlands) 8 practices were selected and invited to participate in a follow-up project on chronic diseases. The selection was based on the period of participation in the national survey (third and fourth trimester of the 1-year period of data collection) and the location of the practice (south-east part of the country). The reason for selecting this part of the country was that from this region the Department of General Practice of Nijmegen recruits practices for educational and research purposes. One practice (3 general practitioners (GP)) refused participation for reasons of the expected high workload. Two of the 7 participating practices are single-handed, 4 have 2 GPs and 1 is a group practice with 5 GPs. In 1988, 56% of the Dutch GPs worked in single-handed practices, 30% in duo-practices and 14% in group practices or health centers. Three of the participating practices are involved in vocational general practice training, the others have no special relationship with a university department of general practice.

In each practice an age/sex register was compiled with the help of trained students. On 1 January 1988 the 7 practices covered 23,534 people. Table 3.1 lists some population characteristics for these practices compared with the total population of The Netherlands.

Information on the distribution in the population of the practices of risk factors for chronic diseases, like body weight, blood pressure, cholesterol, nutrition and smoking habits, is not available.

Identification of cases

In each practice the general practitioners were asked to identify from the practice list all patients with any of the following diseases:

- hypertension
- chronic ischemic heart disease (angina pectoris, previous myocardial infarction, coronary sclerosis) (CIHD)
- diabetes mellitus
- chronic nonspecific lung disease (asthma, chronic bronchitis, emphysema) (CNSLD)
- osteoarthritis of hip and/or knee.

Criteria for identification were: the patient was currently known by the GP or by notation on the patient's record as having any of the chronic diseases mentioned and the diagnosis was made before 1 January 1988. Identification of patients was a two-step process.

Firstly, identification was made on the occasion of an encounter, a repeat prescription or other administrative reason for one of the chronic diseases during the first 3 months of the study, resulting in 1073 patients. In the second step the GP reviewed systematically the patient records of all patients on the practice list who had not had contact with the practice during the previous 3 months. Another 916 patients were identified in this way, resulting in a total number of 1989 patients with 2295 diseases. These figures imply the presence of more than one of the chronic diseases in 1 out of 6 patients. At the time of the identification of patients the GPs were not aware of the aim

of the study, nor had they discussed the diagnostic criteria.

Table 3.1. Characteristics of the population of the 7 study practices (N=23,534) compared to the population of The Netherlands (N=14,714,948) on 1 January 1988; percentages

Population characteristics	Study practices	The Netherlands
Age		
0-4	5.4	6.1
5-14	12.9	12.4
15-24	17.3	16.8
25-44	35.8	31.9
45-64	19.3	20.4
≥ 65	9.3	12.5
Sex		
Male	48.8	49.4
Female	51.2	50.6
Health care insurance (income-related)		
Healt Care Fund members	68.6	61.0
Privately insured or not insured persons	31.4	39.0
Country of birth		
The Netherlands	97.1	96.0
Turkey/Marocco	0.3	2.0
Other Western countries	0.9	1.2
Other non-Western countries	1.7	0.8
Highest educational level (only persons ≥ 18: 72.4%)		
No education/primary school	26.2	20.9
Secondary school	61.9	62.8
University	11.9	16.3
Socio-economic class (profession) (missing data: 25.6 %)		
Brain work: high/middle	23.8	26.1
Brain work: low class	20.9	24.4
Farmers / independent business	8.3	5.7
Hand work: high/middle	23.9	21.5
Hand work: low class	23.2	22.3

Information on diagnostic procedures

In a questionnaire for each patient and each disease the GPs were asked to supply: the diagnostic procedures used, the date of diagnosis, and the diagnosing physician (GP or specialist). They were asked to consult all available sources of information such as patients' records and archives. In answering the questions the GPs were instructed that any "Yes" had to be based on written information on patient history, physical examination or diagnostic tests. Any available information was considered relevant for this study as the diseases involved are chronic and lasting. In collecting these retrospective data we set no limitation in time.

The questions regarding the diagnostic procedures were derived from the ICHPPC-2 diagnostic criteria as is shown in Table 3.2.

Table 3.2. ICHPPC-2 diagnostic criteria and corresponding questions per disease

ICHPPC-2 diagnostic criteria	Questions
Hypertension	
• Blood pressure at two readings > 160/95 mm Hg	• Date encounters? • Blood pressure (mm Hg)?
Chronic ischemic heart disease	
• Old myocardial infarction history, ECG or X-ray evidence • Chest pain compatible with angina pectoris • ECG evidence of myocardial ischemia or ventricular aneurysm • X-ray evidence of narrowed coronary arteries or ventricular aneurysm	• Diagnosis based on - history (Y/N)? - ECG (Y/N)?
Diabetes mellitus	
• Blood glucose level: - fasting ≥ 8.0 mmol/l - not fasting ≥ 11.0 mmol/l • Classic symptoms	• Blood glucose level (mmol/l)? • Condition at the time of taking the sample: (fasting, 2 h after meal, glucose tolerance test, arbitrary occasion)?
CNSLD / Asthma	
• Variable obstruction at pulmonary function test • Wheeze, dry cough, prolonged expiratory phase	• Diagnosis based on - history (Y/N)? - physical examination (Y/N)? - pulmonary function test (Y/N)? - X-ray (Y/N)?
CNSLD / Chronic bronchitis	
• History of cough with purulent sputum • Scattered rales or ronchi on auscultation	• See Asthma
CNSLD / Emphysema	
• X-ray evidence • Obstruction at pulmonary function test • Dyspnea • Shape of chest with reduced breath sounds	• See Asthma
Osteoarthritis hip/knee	
• X-ray evidence • Joint disorder with - irregular swelling - crepitation - stiffness/limited movement - normal laboratory test - age	• Diagnosis based on - history (Y/N)? - physical examination (Y/N)? - laboratory test (Y/N)? - X-ray (Y/N)?

Validity measure

A measure of validity for each chronic disease was determined by comparing the reported procedures with the diagnostic criteria. Agreement with the diagnostic criteria is categorized (Table 3.3):

(a) full agreement (true positive)
(b) partial agreement
(c) no agreement (false positive).

This measure of validity was used for analysis on case level. If no data on the diagnostic criteria were available, the case was designated as "missing". The ICHPPC-2 diagnostic criteria for diabetes mellitus and hypertension list cut-off points of numeric values. For the other diseases the criteria are of a descriptive nature, allowing only a qualitative judgement of the diagnostic validity.

Table 3.3. Categories of agreement with the diagnostic criteria

Full agreement	Partial agreement
Hypertension	
• DBP ≥ 95 mm Hg at two encounters	• DBP ≥ 95 mm Hg at one encounter
Chronic ischemic heart disease	
• Diagnosis based on ECG	• Diagnosis based only on history
Diabetes mellitus	
• Blood glucose level: - fasting: ≥ 8,0 mmol/l or - not fasting: ≥ 11,0 mmol/l	not categorized
CNSLD	
• Diagnosis based on pulmonary function test or X-ray	• Diagnosis based only on history and physical examination
Osteoarthritis hip / knee	
• Diagnosis based on laboratory test or X-ray	• Diagnosis based only on history and physical examination

General practitioner's diagnostic quality

Data on diagnostic procedures performed in diagnosing chronic diseases in patients of any one GP have to be considered interdependent: the diagnostic process is likely to be a physician characteristic rather than a patient characteristic. Consequently, the validity measures for the different chronic diseases are aggregated on the GP level [11]. A diagnostic quality measure was computed by dividing the number of true positive cases by the total number of identified cases per general practitioner, expressed in percentages. The influence of characteristics of GP (gender) and practice (practice type, distance between practice office and nearest hospital, and urbanization level of the community in which the practice is located) on this diagnostic quality measure is analyzed by means of subgroup analysis, comparing means in subgroups by univariate analysis and by calculating the statistical significance with the 2-tailed probability at the

5% level.

Prevalence

The prevalences reflect point-prevalences: the number of disease cases per 1000 in the population on 1 January 1988. As the information on morbidity was derived from general practice records, the time period for measuring prevalence for each patient was potentially lifelong. The mean duration of the diseases on 1 January 1988 varied from 4 to 9 years.

The prevalences of the chronic diseases are based on the diseases of the identified patients ("unadjusted" prevalence). Adjustment was carried out by only taking into account true positive cases.

3.3. Results

The cooperation of the GPs was satisfying, considering the intensive search for data in archives and patient files that had to be made. No data about the applied criteria could be traced in 17 % of the diagnoses. In 5 % of the diagnoses it is unknown whether it was made by a GP or by a specialist.

Validity of diagnoses

Table 3.4 shows the agreement of the applied procedures with the ICHPPC-2 diagnostic criteria for all cases diagnosed by GPs (63% of all diagnoses). The agreement is high in cases of diabetes mellitus (96% true positive cases), hypertension (85%) and osteoarthritis (81% true positive). Partial agreement is a substantial category in CIHD and CNSLD. The category "no-agreement with the diagnostic criteria" (the false positive cases) is highest in diabetes mellitus (4%).

Table 3.4. Agreement of the performed diagnostic procedures with the diagnostic criteria (in percentages of the cases for each disease) - only cases diagnosed by the GP

	No. of cases (abs)	Agreement			Missing data (abs)
		Full %	Part %	No %	
Hypertension	(719)	85.1	12.6	2.3	(75)
Chronic ischemic heart disease	(194)	67.9	29.9	2.2	(10)
Diabetes mellitus	(172)	96.1	-	3.9	(44)
Chronic nonspecific lung disease	(292)	57.6	42.4	0.0	(35)
Osteoarthritis hip/knee	(68)	80.6	19.4	0.0	(6)

In patients whose diagnosis was made by a specialist (results not shown) data is often missing, especially in hypertension and diabetes mellitus. The specialists' diagnoses in patients with CIHD and CNSLD are more in agreement with the ICHPPC-2 criteria than cases diagnosed by GPs (85 vs 68% and 81 vs 58%, respectively). In

diabetes mellitus diagnosed by specialists the agreement is lower (82 vs 96% in GPs' diagnoses).

Diagnostic quality

In Table 3.5 the diagnostic quality measures of the participating GPs are summarized. The general practitioners diagnosed hypertension, diabetes mellitus, ischemic heart disease and osteoarthritis in more than 70 % of the cases in full agreement with the criteria; in chronic lung disease the diagnostic quality is lower. The relatively small confidence intervals in diabetes mellitus and hypertension indicate little variation between the general practitioners.

Further analysis of the diagnostic quality measure in subgroups defined by GP and practice characteristics shows significant differences ($p < 0.05$) only on the variables "single-handed and duo practice" vs "group practice" (GPs from the group practice scored lower in CIHD and CNSLD) and urbanization level of the community served (GPs in suburbanized communities scored lower for CIHD and CNSLD). There was no correlation between the diagnostic quality ratios for the different diseases for the individual GP (data not shown).

Table 3.5. Mean diagnostic quality (percentage of true positive cases) of the participating general practitioners ($N=15$) per chronic disease. Percentages and 95% confidence intervals

	No. of patients (abs)	True positive (%)	95% CI
Hypertension	(644)	85.5	81.0-90.1
Chronic ischemic heart disease	(184)	76.3	58.4-94.3
Diabetes mellitus	(128)	97.6	95.6-99.6
Chronic nonspecific lung disease	(257)	62.5	44.3-80.7
Osteoarthritis of hip/knee	(62)	84.0	71.1-96.8

Prevalence

Table 3.6 summarizes the prevalence of the chronic diseases, regardless of whether the diagnosis was made in general practice or by a specialist, in relation to agreement with the diagnostic criteria. The prevalence rates are computed for two age-groups: $<$ 65 and $\geq$ 65 years old. Adjustment by only including true positive cases lowers the prevalence of all chronic diseases.

Table 3.6. Point-prevalence and 95% confidence intervals unadjusted and adjusted (true positive cases only) in people < 65 (N=21,349) and ≥ 65 years (N=2185) of 5 chronic diseases in the study practices per 1000 patients

	< 65 years			
	Unadj.	95% CI	Adj.	95% CI
Hypertension	24.7	22.6-26.8	18.5	16.6-20.3
Chronic ischemic heart disease	10.9	9.5-12.3	7.5	6.4-8.7
Diabetes mellitus	7.3	6.1-8.4	4.3	3.4-5.1
Chronic nonspecific lung disease	19.9	18.0-21.0	12.2	10.8-13.7
Osteoarthritis hip/knee	2.2	1.5-2.8	1.7	1.1-2.2
	≥ 65 years			
	Unadj.	95% CI	Adj.	95% CI
Hypertension	143.2	129.0-158.0	89.7	78.1-102.0
Chronic ischemic heart disease	100.2	87.6-113.0	75.1	64.4-86.9
Diabetes mellitus	60.9	51.2-71.7	33.0	25.8-41.3
Chronic nonspecific lung disease	65.4	55.5-76.6	43.5	35.3-52.9
Osteoarthritis hip/knee	38.0	30.3-46.8	29.3	22.6-37.3

3.4. Discussion

Validity

Diagnoses of chronic diseases made by GPs agree very well with the diagnostic criteria of the ICHPPC-2-Defined. The highest rate of false positive cases is 4% (diabetes mellitus).

In the case of diabetes mellitus, it should be taken into account that the widely used diagnostic criteria changed in 1980 to more stringent ones [12]. In this study 4 out of the 14 false positive cases of diabetes mellitus were diagnosed before 1980.

The number of cases with CIHD and CNSLD diagnosed on the basis of history and physical examination ("partial agreement") is relatively high. This reflects the common diagnostic procedures in general practice in The Netherlands where electrocardiographic and spirometric examinations are not available in general practice. Apparently GPs consider the patient's history, and signs and symptoms at physical examination to be a sufficient basis for diagnosing these cardiac and respiratory diseases.

For many patients osteoarthritis is a silent disease: only patients with complaints or symptoms consult a GP, and the GP will only report on these cases. Consequently, in this study probably only osteoarthritis patients with complaints were included as being "at risk" for undergoing X-ray examination. This is reflected in the high percentage of

true positive cases of osteoarthritis.

The number of missing data is acceptable, considering the retrospective nature of the collected data. Moreover, for the diagnoses made by medical specialists, it should be kept in mind that patients in The Netherlands will only come under the care of a specialist upon referral by a GP. The medical specialist usually reports his diagnosis to the GP, but does not always include the criteria upon which the diagnosis is based.

Routine general practice care does not necessarily imply detailed documentation of performed diagnostic procedures. As this study is based on recorded evidence the level of agreement with diagnostic criteria is an underestimation of validity. The "partial agreement" category, for example, probably includes a number of true positive cases. This could be verified by performing additional diagnostic procedures. Moreover, we have no information on false negative cases.

We suggest that agreement with international standard diagnostic criteria for general practice is the best way to assess the validity of the diagnosis. The diagnostic criteria of the ICHPPC-2-Defined seem to be useful in assessing the quality of diagnoses, although difficult to use in qualitative retrospective data. Operationalization of these criteria for use in research needs further elaboration.

Diagnostic quality

The diagnostic quality per chronic disease varies substantially between the GPs. When the results on validity are aggregated from the patient level to the level of the GP the mean percentages do not change very much. The confidence intervals, however, are larger because of the sample size (15 GPs). This is especially the case for CIHD and CNSLD, which is possibly explained by differences between general practitioners in the use of clinical diagnostic facilities (electrocardiography and spirometry).

We find no support in our data for the assumption that there is a general diagnostic ability of GPs reflected in a correlation between the quality ratios for different diseases, but the number of general practitioners in our study is too small for definitive conclusions.

Prevalence

Substantial differences in prevalences are found by adjustment for true positive cases only, mainly due to the number of missing cases left out. The age-specific adjusted prevalence rates of the chronic diseases are lower in this study than those in other morbidity surveys in general practice in The Netherlands [13,14]. On the patient level our sample can be considered representative for the entire population of The Netherlands. On the level of practices the sample is too small to allow generalization.

For chronic lung disease the differences in prevalence in morbidity surveys reflect the differences in definition between The Netherlands and the U.K. [15,16].

Osteoarthritis of hip and/or knee is probably the most underreported chronic disease in this study, because only patients with complaints are seen. Comparison with other morbidity data is difficult as generally all cases of osteoarthritis are reported without specifying the affected joints.

These discrepancies can be explained by differences between GPs in registration discipline [17], differences in case-finding, differences in applying diagnostic criteria or by real morbidity differences between populations. We have no information about applied diagnostic criteria in these large surveys. We have no reason to suppose that

the population of our study practices differs that much from other populations that the studied diseases really occur less frequently.

3.5. Conclusions

Diagnoses of the 5 chronic diseases recorded in general practice are generally valid with low numbers of false positive cases. The diagnosing physician as source of variability in the validity of diagnoses should not be ignored. The validity of morbidity data originating from population surveys can well be measured by comparison with GPs' records.

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4. Comorbidity of chronic diseases in general practice

... The 'doctrine of the single diagnosis' found no place in the interpretations of these diseases, characterised as they were by their multiplicity...•

Abstract - *With the increasing number of elderly people in The Netherlands the prevalence of chronic diseases will rise in the next decades. It is recognized in general practice that many older patients suffer from more than one chronic disease (comorbidity). The aim of this study is to describe the extent of comorbidity for the following diseases: hypertension, chronic ischemic heart disease, diabetes mellitus, chronic nonspecific lung disease, osteoarthritis. In a general practice population of 23,534 persons 1989 patients have been identified with one or more chronic diseases. Only diseases in agreement with diagnostic criteria were included. In persons of 65 and older 23% suffer from one or more of the chronic diseases under study. Within this group 15% suffer from more than one of the chronic diseases. Osteoarthritis and diabetes mellitus are the diseases with the highest rate of comorbidity. Comorbidity restricts the external validity of results from single-disease intervention studies and complicates the organization of care.*

• *Wilson LA, Lawson IR, Brass W. Multiple disorders in the elderly. Lancet 1962;ii:841-843.*

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4.1. Introduction

The morbidity pattern in general practice is well-documented, particularly in The Netherlands and in the U.K., where the fixed practice population allows for population-based description [1-4].

General practice covers its own clinical spectrum as has been demonstrated previously [5]. Chronic diseases are an important feature of this clinical spectrum: hypertension, chronic ischemic heart disease, diabetes mellitus, chronic nonspecific lung disease, and osteoarthritis all have a prevalence above 10 per 1000 and are mostly managed in general practice [3,4,6,7]. In the near future the number of elderly people will increase in the Netherlands. As a consequence, the prevalence of chronic diseases will rise.

These changes in morbidity pattern will influence the daily work in general practice. Standards and guidelines for proper diagnosis, treatment and management of chronic diseases are crucial for maintaining the quality of care. Intervention studies provide an essential basis for adequate treatment and prevention. Most of such studies analyze the effects of intervention on a single disease. General practitioners (GPs), however, recognize that their patients often suffer from more than one chronic disease. As a generalist the GP, alone or in cooperation with the specialist, deals with all diseases of a patient. As the natural course and the therapeutic interventions of one disease will influence the co-existing second (or even third) disease [8], comorbidity diminishes the practical value of single-disease standards for treatment and management, derived from single-disease trials. We found no publications on the frequency of comorbidity in general practice populations. The aim of this study is to describe the extent of comorbidity of chronic diseases in general practice in The Netherlands: how many of the patients are under care for more than one of the following, most common, chronic diseases: hypertension, chronic ischemic heart disease, diabetes mellitus, chronic nonspecific lung disease, and osteoarthritis?

The findings indicate the prevalence of these problems and thus contribute to our insight in disease clustering [9].

4.2. Methods

This study is part of a larger research on the prevalence of chronic diseases in general practice, and of the effects of systematic surveillance on the quality of care.

General practices and population

Seven general practices (15 GPs) participated in the study. The practices covered 23,534 persons at the start of the data collection (1 January 1988). An age/sex register of the practices was completed with the help of trained students. The number of persons of 65 years and over is 3% less than in the entire country (9.3 vs 12.5% - Table 4.1). For that reason all results are presented for two subpopulations: that of persons below 65 and that of persons of 65 and over. In other characteristics the practice population differs only marginally from the entire population [10].

Case identification

The participating GPs identified all patients known to them with the following diseases:

- hypertension
- diabetes mellitus
- chronic ischemic heart disease (CIHD) (angina pectoris, previous myocardial infarction, coronary sclerosis)
- chronic nonspecific lung disease (asthma, chronic bronchitis, emphysema) (CNSLD)
- osteoarthritis of hip and/or knee.

Identification took place on the occasion of a consultation, a repeat prescription or another administrative reason for visiting the practice during the first three months. Finally, the general practitioner reviewed systematically all patient records to identify diseases of patients who were not seen.

This process of identification resulted in a total number of 1989 patients with 2295 diseases (cases).

Table 4.1. Age and sex distribution of the population of the general practices studied (N=23,534) compared to the population of The Netherlands (N=14,714,948) 1 January, 1988

	Practice population (%)	The Netherlands (%)
0-4	5.4	6.1
5-14	12.9	12.4
15-24	17.3	16.8
25-44	35.8	31.9
45-64	19.3	20.4
≥ 65	9.3	12.5
Male	48.8	49.4
Female	51.2	50.6

Application of diagnostic criteria

The GP provided retrospective data of the medical history from the patients' records in relation to the diagnostic procedures applied in diagnosing the chronic disease, regardless of whether the diagnosis was made in general practice or by a medical specialist. These data were compared with the inclusion criteria of the International Classification of Health Problems in Primary Care [10,11]. Only the cases (diseases) meeting these inclusion criteria were used for analysis.

Analysis

Comorbidity of chronic diseases is defined as the "point-prevalent concurrence" of the studied diseases known to the participating GPs. Point-prevalence reflects the number of diseases in the population at 1 January 1988. Comorbidity was analyzed on patient level by means of the multiple response technique in SPSS [12]. Comorbidity is expressed as the number of the studied diseases per patient, the mean number of

diseases per patient in each disease category, and the proportion of patients with at least one of the other diseases. Due to the cross-sectional measurement and the method of presentation, patients with comorbidity appear in each of the disease categories that apply to them and are therefore counted more than once (e.g. a patient with diabetes and with hypertension appears in the hypertension group as well as in the diabetes category). Proportions and means are presented with the 95% confidence intervals (CI).

4.3. Results

Our definition of comorbidity is strongly connected with the prevalences of the studied diseases. Table 4.2 lists the point-prevalences on January 1, 1988 of the diseases meeting the inclusion criteria. The prevalence of most diseases is high in persons over 65. Hypertension is the most frequent of the studied diseases. Table 4.3 shows the distribution of the number of the diseases per patient. In the younger subgroup there are few persons known to have one of the studied diseases, and comorbidity occurs in only 0.3% of these persons. Of the persons over 65 years old, more than 75% are known not to have one of the 5 chronic diseases, but of the older patients who do have one of these diseases, 16% has more than one chronic disease.

Table 4.2. Point-prevalence in persons < 65 (N=21,349) and ≥ 65 (N=2185) of 5 chronic diseases per 1000 persons in the general practices studied

	< 65		≥ 65	
	Prevalence	95% CI	Prevalence	95% CI
Hypertension	18.5	16.6-20.3	89.7	78.1-102.0
CIHD	7.5	6.4-8.7	75.1	64.4-86.9
Diabetes mellitus	4.3	3.4-5.1	33.0	25.8-41.3
CNSLD	12.2	10.8-13.7	43.5	35.3-52.9
Osteoarthritis hip/knee	1.7	1.1-2.2	29.3	22.6-37.3

Table 4.3. Number of studied chronic diseases per person in the population of the general practices

Number of chronic diseases	< 65 (N=21,349) (%)	≥ 65 (N=2185) (%)
None	95.9	76.9
One	3.8	19.5
Two	0.3	3.2
Three	<0.1	0.3
Four	-	<0.1

Tables 4.4 (A) and (B) show the extent of comorbidity in patients with at least one disease for the two age groups. In patients under 65 years old patients with osteoarthritis have the highest rate of comorbidity. The most frequent second disease in these patients is CNSLD (5 of 36 patients). In diabetics under 65 (N=91) hypertension is the most frequent second disease (15%). In patients of 65 years and older the highest frequency of comorbidity is found in patients with diabetes mellitus. The most frequent second chronic disease in diabetics over 65 is CIHD (22%), followed by hypertension (19%). High rates of comorbidity are also found in patients with osteoarthritis (mostly hypertension and CNSLD) and CIHD (mostly hypertension).

Table 4.4 (A). Extent of comorbidity per disease for patients < 65, presented as number of chronic diseases per patient group and as fraction of patients with comorbidity per patient group

		Number of chronic diseases per patient		Fraction of patients with comorbidity
	N	Mean	95% CI	% of N
Hypertension	394	1.1	1.07-1.13	9.6
CIHD	161	1.2	1.14-1.28	19.9
Diabetes mellitus	91	1.2	1.13-1.33	20.9
CNSLD	250	1.1	1.04-1.11	7.6
Osteoarthritis hip / knee	36	1.3	1.12-1.43	27.8

Table 4.4 (B). Extent of comorbidity per disease for patients ≥ 65, presented as number of chronic diseases per patient group and as fraction of patients with comorbidity per patient group

		Number of chronic diseases per patient		Fraction of patients with comorbidity
	N	Mean	95% CI	% of N
Hypertension	196	1.3	1.18-1.32	21.9
CIHD	164	1.3	1.24-1.42	28.0
Diabetes mellitus	72	1.5	1.32-1.62	40.3
CNSLD	93	1.3	1.18-1.42	24.7
Osteoarthritis hip/knee	64	1.4	1.22-1.50	32.8

CIHD = chronic ischemic heart disease; CNSLD = chronic nonspecific lung disease.

4.4. Discussion

Prevalence of chronic diseases

This study is based on data obtained from medical records. Generally this leads to an underestimation of the number of cases in the population. Moreover, only cases in agreement with diagnostic criteria were included. The prevalence of hypertension, chronic ischemic heart disease, diabetes mellitus, and chronic nonspecific lung disease is lower than in other Dutch reports from general practice [3,4]. Compared with data from the U.K., the prevalence of diabetes mellitus is higher, as has been reported by others [13].

Chronic nonspecific lung disease has been identified as an area of diagnostic confusion. Differences in opinion between physicians in the U.K. and The Netherlands exist as to whether asthma, chronic bronchitis and emphysema have the same pathophysiological characteristics, the so-called Dutch hypothesis, which is heavily disputed [14,15]. As Dutch GPs are familiar with the diagnostic label of chronic nonspecific lung disease, this term is used in our description of comorbidity.

Extent of comorbidity

Comorbidity is a quantitatively important phenomenon in patients over 65 with a chronic disease. Most people over 65 (77%) do not suffer from any of the 5 most common chronic diseases, but within the affected group 16% is known to suffer from at least one other of the 5 chronic diseases studied.

The occurrence by chance of two diseases in one person can be estimated by multiplying the prevalences of the separate diseases. The observed comorbidity of the five diseases under study is significantly higher. Having a chronic disease apparently means being at higher risk to have a second or even third disease.

By including only diagnoses meeting diagnostic criteria and by disregarding false negative diagnoses we probably underestimate also the extent of comorbidity. Moreover, these figures are related only to the 5 chronic conditions under study. The rate of comorbidity would have been even larger, if additional diseases, like malignant neoplasms, epilepsy and other neurological diseases, stroke, peripheral vascular disease, peptic ulcer disease, had been considered. On the other hand, by estimating the extent of comorbidity in a general practice setting bias due to the Berkson's fallacy cannot be excluded: patients under care for a chronic disease are at higher risk for detection of diseases than persons who do not receive such care.

Comorbidity is partly the result of a common pathophysiological process or of complications in the natural course of a disease, as is the case for diabetes mellitus and cardiovascular disease [16]. In other cases, comorbidity of chronic diseases is accidental and cannot be explained pathophysiologically.

4.5. Consequences

Persons suffer from more than one chronic disease more frequently than could be expected by chance from the prevalence of the disease in the general population. This is a clinical reality of medical practice with consequences for research and for the

organization of daily care.

Research

Optimal patient care should ideally be based on valid results from clinical trials. In intervention studies, however, patients with comorbidity often are excluded in the selection of a study group, e.g. in the well-known therapeutic trials in hypertension [17,18]. This selection restricts the external validity of the results for excluded patient categories, as has recently been described for the elderly and women [19,20]. The existence of a second disease complicates the choice of the antihypertensive treatment that is proven to be effective in single disease patients (e.g. diuretics in diabetes, bèta-blockers in lung disease). Strictly speaking, these studies have not proven the effectiveness of antihypertensive treatment in lowering blood pressure and decreasing cardiovascular morbidity and mortality for patients with comorbidity. In intervention studies on treatment of chronic diseases patients with comorbidity should be included. In analyzing the data patients with comorbidity can be handled as a subgroup, or adjustment of the results for comorbidity can be carried out.

The specific combinations of chronic diseases need further exploration, in order to gain more insight into patterns of disease clustering and hypothetically common etiology.

Care

Systematic surveillance of patients with chronic diseases is essential in order to provide them with optimal care [7]. Patients with more than one chronic disease are at risk of being included in more than one surveillance scheme. This should be recognized when designing surveillance programs, since it would be counter-productive to have patients visit the practice on various different occasions, as a result of following different schemes for each of their diseases. Careful registration of all diseases is conditional not only for organizational reasons but also for the care to be provided.

Chronic diseases are regarded as "the very stuff of general practice" [6]. Proper management of patients with comorbidity of chronic diseases presents a real challenge to the GP.

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5. Influence of comorbidity of chronic diseases on workload

A study of patients with chronic diseases in general practice

... Medical science and medical education should be inspired by diseases of general practice ...[*]

Abstract - *Consultation rates and incidence rates of intercurrent morbidity were studied in general practice in five cohorts of patients with common chronic diseases: hypertension, chronic ischemic heart disease, diabetes mellitus, chronic respiratory disease, and osteoarthritis. In 7 practices with 15 general practitioners the records of all patients were screened for inclusion in the study. Data used for analysis are from 962 patients, whose diagnoses were made in agreement with diagnostic criteria, who were not under specialist care, and who were followed up for 21 months. A distinction was made between patients with one or two or more of the five studied chronic diseases. For the single-disease subgroups of hypertensive patients and of diabetics two reference groups of persons without a chronic disease, standardized for age and sex, were composed from the population in the same practices. Consultation rates tended to be higher for patients with comorbidity than for single-disease patients. Patients in the reference groups tended to have lower consultation rates than the comparable single-disease groups. Intercurrent diseases were presented more frequently to the general practitioner by patients with comorbidity than single-disease patients. Patients with only hypertension had lower total incidence rates of intercurrent morbidity than their comparable reference group. Most intercurrent morbidity consisted of acute common diseases as myalgia, upper respiratory tract infection and urinary tract infection. Patients with only hypertension or only diabetes had higher consultation rates but had no higher total incidence rates of intercurrent morbidity which is in contrast to the so-called Berkson's fallacy.*

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[*] *Buma JT. De huisarts en zijn patient. Amsterdam: Allert de Lange Universiteitspers, 1950.*

Schellevis FG, Lisdonk EH vd, Velden J vd, Hoogbergen SHJL, Eijk JThM v, Weel C v. The influence of comorbidity of chronic diseases on workload. A study of patients with chronic diseases in general practice [Submitted].

5.1. Introduction

In the Netherlands chronic diseases are primarily managed by general practitioners (GPs). This care includes the diagnostic and therapeutic activities in the initial phase as well as the long term management of the disease [1]. It is expected that GPs will have to care for more patients with chronic diseases in the near future. This is the consequence of an increase in the number of elderly people and of political measures emphasizing primary care. Insight into the workload generated by the care of patients with chronic diseases, is relevant for the management of chronic diseases in general and for the organisation of general practice in the future.

This study analyses the consultation rates and the number and nature of intercurrent morbidity presented to the GP by five cohorts of patients with the following, most common chronic diseases: hypertension, chronic ischemic heart disease, diabetes mellitus, chronic respiratory disease, and osteoarthritis. In a previous study we found a considerable number of patients with combinations of two or more of these five chronic diseases, which is referred to as 'comorbidity' [2]. Therefore, the influence of comorbidity on consultation rates and intercurrent morbidity justifies special attention. In this study the following questions are dealt with:

* What are the differences in consultation rates between patients with a single chronic disease and patients with comorbidity of chronic diseases?
* What are the incidence and nature of intercurrent morbidity in these patient groups?

5.2. Methods

Design

Five cohorts of patients were followed for 21 months. Intercurrent morbidity of patients with chronic diseases is potentially influenced by the phenomenon described by Berkson [3], indicating a higher chance of diagnosing diseases in patients who are already under care than in patients who do not consult their GP. For this reason reference groups of persons without a chronic disease were included in the analysis.

Selection of practices and patients

Study cohorts

The selection of practices and patients has previously been described in detail [4]. In summary, seven practices (15 GPs) were selected following their participation in the Dutch National Survey of General Practice [5]. The total practice population consisted of 23,534 persons at the start of the study. The GPs identified all patients in their practices, known to have at least one of the following diseases:

- hypertension
- chronic ischemic heart disease (CIHD)
- diabetes mellitus
- chronic respiratory disease (asthma, chronic bronchitis, emphysema)
- osteoarthritis of knee and/or hip.

This identification procedure resulted in a total number of 1989 patients. Background

data were collected for each patient and each chronic disease on the diagnostic procedures performed in diagnosing the chronic disease, the date of the diagnosis, and the physician responsible for the follow-up care. Five cohorts for the above mentioned chronic diseases were defined on the basis of the following three criteria:

- diagnosis made before 1 January 1988 (the start of the study period)
- diagnosis in agreement with the diagnostic inclusion criteria of the ICHPPC-2-Defined [6]
- the patient is not receiving follow-up care for the chronic disease from a specialist at the start of the study.

The last requirement ensured that all morbidity during the study period was presented to the GP, because in The Netherlands medical specialists can only be consulted after referral by a GP. Application of these criteria left a total number of 962 patients who were included in the analysis. Table 5.1 presents characteristics of these patients.

Table 5.1. Background characteristics of patient cohorts

	Hyper-tension	Chronic ischaemic heart disease	Diabetes Mellitus	Chronic respiratory disease	Osteo-arthritis
N of patients	549	183	119	243	80
males (%)	35	62	42	60	33
mean age (yrs)	60	67	65	45	69
single-disease (%)	86	74	69	89	69

Within the defined cohorts there were patients known to have only one disease and patients known with comorbidity at the start of the study. Comorbidity is defined as the "point-prevalent concurrence of two or more of the five studied chronic diseases" [2]. On this basis each cohort was divided in a *single-disease* and a *comorbidity* subgroup.

Reference groups

Two separate reference groups of persons without a chronic disease were composed for the single-disease subgroups of the hypertension cohort and the diabetes cohort. Hypertension and diabetes were chosen because in The Netherlands these patients are usually included in a surveillance scheme for regular control visits, thus allowing to subtract the usual number of control visits per year from the consultation rates in order to get figures that can be compared with the reference groups. The reference groups were recruited from the population of the same practices. Data used for composing the reference groups originated from the Dutch National Survey of General Practice. Persons with any of the following diseases were excluded: hypertension, diabetes mellitus, chronic ischemic heart disease, chronic respiratory disease (asthma, chronic bronchitis, emphysema), non-vertebral osteoarthritis, stroke, peripheral arterial disease, rheumatoid arthritis, any malignant neoplasm, and dementia. The reference groups were standardized for age and sex relative to either the single-disease hypertension subgroup or the single-disease diabetes subgroup. The reference group for the hypertension subgroup consisted of 14,623 persons, the diabetes reference group of 15,847

persons.

Measurements

Study cohorts

During the study period all consultations were registered by the GPs on special research forms. For each consultation the GP registered one or more diagnoses at the most appropriate highest diagnostic level [7]. These diagnoses were coded by trained clerks according to the International Classification of Primary Care (ICPC) [8]. In case of more than one consultation for the same diagnosis, the consultations were clustered by the same clerks into episodes of disease ("a problem or illness in a patient, over the entire period of time from its onset to its resolution" [9]). The episode diagnosis was characterised by the diagnosis of the last registered consultation during the episode, as is usual in general practice morbidity studies [10,11]. Whether the episode was 'new' (never presented before) or 'old' (already existing at the start of the study period) was indicated on the research form at the first consultation for each episode. For this paper only episodes of disease were included that had started during the study period, while episodes in progress at the start of the study were ignored.

Reference groups

Data on consultations and intercurrent morbidity of the reference groups originated from the Dutch National Survey of General Practice. The data of the reference groups were collected during the three months preceding the data collection in the study cohorts. Measurement of the number of consultations and construction of disease episodes was carried out identically as described for the study cohorts.

Measures

The number of consultations and the number of disease episodes were all rescaled to rates per annum. The *consultation rate* reflects the total number of consultations (face-to-face contact with the GP at the practice or at home) per year, irrespective of the presented morbidity. Consultation rates are presented as means for the single-disease subgroup and for the comorbidity subgroup of each cohort. *Intercurrent morbidity* reflects episodes of new diseases presented to the GP. Intercurrent morbidity is represented as total incidence rates per 1000 patients per year. Intercurrent morbidity was also studied at the level of ICPC-chapter and at the level of diagnoses.

Reliability and validity of data on the study cohorts

In one practice (2 GPs) the registration was interrupted for 3 months due to reorganization of the practice. Correction for this interruption was made in the calculation of the consultation rates and the incidence rates for each cohort.

The completeness of the registered number of consultations was checked by comparing all consultations in a sample of 2% of the patients with the regularly used patient charts. Of all consultations mentioned on the charts 70% appeared to be present in our database. This underreporting mainly consisted of consultations for repeat prescriptions and consultations during evenings and weekends. No correction was made for this underreporting.

Agreement on the diagnostic labelling of diseases by the 15 GPs was studied by making a diagnosis in 30 written case histories. The mean inter-observer agreement was

90%.

Analysis

Univariate descriptive analysis was carried out to compute consultation rates and total incidence rates for the different subgroups and the reference groups. Confidence intervals of the means are presented at the 95% level. Data analysis was performed with SPSS-X / SPSS-PC.

5.3 Results

Consultation rates

Table 5.2 shows the consultation rates for the single-disease and for the comorbidity subgroups of each disease cohort. The consultation rates tended to be higher in all comorbidity subgroups than in the single-disease subgroups. The largest differences were found in patients with chronic respiratory disease, and those with osteoarthritis, where the consultation rates in the comorbidity subgroups were 51% and 52% higher, respectively, than in the single-disease subgroups. However, the comorbidity subgroups in these cohorts were both small (N=27, N=25, respectively). The confidence intervals were large for all estimated means, indicating high individual variation in consultation rates. Patients in the reference groups without a chronic disease had a mean consultation rate of 3.0 and 2.8, while the single-disease hypertensive and single-disease diabetic patients showed rates of 4.7 and 5.7, respectively. In The Netherlands hypertensive and diabetic patients usually visit their GP two to four times a year for control of their chronic disease.

Table 5.2. Consultation rates in five disease cohorts (means and 95% confidence intervals) for single-disease, comorbidity, and reference group

	Single-disease mean (95% CI)	Reference mean (95% CI)	Comorbidity mean (95% CI)
Hypertension	4.73 (4.43-5.04)	2.97 (2.88-3.06)	5.44 (4.30-6.58)
Chronic ischemic heart disease	5.46 (4.67-6.24)		6.04 (4.78-7.30)
Diabetes mellitus	5.66 (4.91-6.42)	2.81 (2.73-2.89)	6.54 (4.65-8.44)
Chronic respiratory disease	4.90 (4.27-5.53)		7.40 (5.01-9.80)
Osteoarthritis	4.24 (3.23-5.24)		6.43 (4.90-7.96)

Intercurrent morbidity

Total incidence rates of intercurrent morbidity for the subgroups of the five cohorts are listed in Table 5.3. In all cohorts patients with comorbidity tended to have higher total incidence rates of intercurrent morbidity than the corresponding single-disease patients, varying from 8% for diabetics to 74% for osteoarthritis patients.
Surpisingly, in case of the hypertensive patients, the total incidence rate for the

reference group was 42% higher than for the corresponding single-disease group. The difference between the total incidence rates of the single-disease diabetics and their reference group without a chronic disease is unimportant.

Table 5.3. Intercurrent morbidity in five disease cohorts for single-disease, comorbidity, and reference groups (total incidence rates per 1000 patients per year)

	Single-disease	Reference	Comorbidity
Hypertension	1247	1776	1645
Chronic ischemic heart disease	1794		2021
Diabetes mellitus	1618	1683	1755
Chronic respiratory disease	1784		2489
Osteoarthritis	1504		2619

Analysis of the incidence rates of intercurrent morbidity at the level of ICPC-chapter showed that the highest rates were found in the chapters K (circulatory), L (musculoskeletal), R (respiratory), and U (urology). No important differences in this pattern were found between the subgroups within each of the five cohorts (data not shown). At the level of diagnoses the five diseases with the highest incidence rates were determined for each single-disease subgroup. Only eight acute diseases appeared with remarkable similarity in all five cohorts: myalgia, upper respiratory tract infection, acute bronchitis, urinary tract infection, influenza, ear wax, pneumonia, and sinusitis. Comparison between the single-disease and comorbidity subgroups showed a trend of higher incidence rates in the comorbidity subgroups of hypertensive patients, of diabetic patients, and of CIHD patients. The reference groups showed clearly lower incidence rates of these acute diseases than the corresponding single-disease subgroups (data not shown).

5.4. Discussion

Consultation rates

The mean consultation rate for all patients in general practice in the Netherlands is 3.2 [12]. The mean consultation rate of patients with a single chronic disease in this study varied from 4.2 to 5.7; for patients with more than one of these diseases it varied from 5.4 to 7.4. Correction for the 30% underreported consultations would further increase these rates. Having more than one of the studied chronic diseases apparently implies more consultations per year than having only one. The consultation rates do not increase linearly with the number of chronic diseases. The rates in the two reference groups were lower than the corresponding single-disease hypertension and diabetes subgroups. Having only hypertension or only diabetes induces higher consultation rates than usual for this age group. Assuming that patients with hypertension and diabetes usually visit their GP two to four times a year for regular control of their chronic

disease, the number of consultations for other reasons seems to be lower compared to patients without a chronic disease. This finding confirms previous results in hypertensive patients [13]. Patients with only hypertension or only diabetes probably present their other problems partially during their control visits. Our results only indicate trends of consultation rates, since the confidence intervals of the means between subgroups show considerable overlap.

Intercurrent morbidity

Another morbidity study in the entire population of four general practices found a total incidence rate of 1681 per 1000 patient years [10]. The figures of the single-disease subgroups and the reference groups in this study are of a corresponding magnitude. The total incidence rates of intercurrent morbidity were lower in the single-disease subgroups than in the comorbidity subgroups. In diabetics the presence of other chronic diseases seemed to have little influence on total incidence rates. The difference between the subgroups was substantial in the cohorts of patients with chronic respiratory disease, and of patients with osteoarthritis: in these patients the presence of other chronic diseases seemed to have an increasing influence on intercurrent morbidity.

Our results confirm an earlier finding that patients with chronic diseases also present 'common diseases' to the GP [14]. It could be argued that patients with chronic diseases would save their problems until the next control visit. This would lead to increased morbidity without increased consultation rates in patients with chronic diseases compared to those without chronic diseases, according to the phenomenon described by Berkson [3]. When we compare intercurrent morbidity incidence and consultation rates for hypertensive patients with the corresponding reference group, we found the reverse effect. Patients with only hypertension or only diabetes, although they consult their GP more frequently, do not present more intercurrent morbidity than persons of the same age without either disease. On the contrary, patients without a chronic disease have even higher rates of total intercurrent morbidity.

It can be expected that patients will particularly more often need care of their GP in the period of terminal illness. However, the number of patients in this study who died during the observation period ($N=17$) was too small to analyze this.

Limitations

The incompleteness of the database of the study group, reflecting 70% of the consultations listed on the patients' charts could not be resolved in a satisfactory way. The fact that the participating GPs had to complete research forms for consultations of only a part of their patients made it difficult for them to do so in all cases. The incompleteness causes an underestimation of the consultation rates. Correction for underestimation by just adding 30% in all groups would ignore possible differences between subgroups with regards to the completeness of their data. Therefore, we have presented the observed figures without correction. This seems to be warranted for two reasons. First, many of the missed consultations were for the purpose of obtaining a repeat prescription. Secondly, we have analyzed intercurrent morbidity at the level of episodes of disease, which decreases the importance of a missed consultation.

In interpreting the results it should be kept in mind that there is an overlap of the comorbidity subgroups from the different cohorts: patients with more than one chronic disease are present in more than one comorbidity subgroup.

Comorbidity is defined here as a combination of two or more of five studied chronic diseases. It depends on the definition of chronicity what proportion of all chronic diseases in a general practice population is represented by the five studied diseases. When the summated prevalence of the diseases used for exclusion in the composition of the reference groups is taken as 100%, the five studied chronic diseases represent about 70% of these. Including other chronic diseases, like gastrointestinal and mental health problems, would of course change the obtained results.

5.5. Conclusion

Patients with chronic diseases have high consultation rates which are even higher when these patients have more than one chronic disease. However, patients with only hypertension or only diabetes do not have high total incidence rates of intercurrent morbidity, suggesting that the Berkson's fallacy plays only a minor role in the figures of these patients. Patients with chronic diseases present also common diseases to the GP. This emphasizes the important role of GPs in the management of all diseases in a single patient.

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6. Performance of general practitioners in the follow-up care of patients with chronic diseases

The implementation of consensus guidelines

... Writing guidelines is easier than making them work ...[*]

Abstract - *The objective of this study was to evaluate the effects of formulating and implementing consensus guidelines on the follow-up care for patients with chronic diseases by general practitioners. Agreement was studied between guidelines reflecting optimal care and the actually delivered care by 15 general practitioners to their patients with hypertension (N=613), chronic ischaemic heart disease (N=76), diabetes mellitus (N=95), chronic respiratory disease (N=115), and osteoarthritis of hip and/or knee (N=17). The participating general practitioners held monthly meetings to reach consensus on guidelines for optimal care. The general practitioners registered data on the care delivered to their patients during 21 months. The implementation of the consensus guidelines was supported by feeding back information on actually delivered care integrated in peer review meetings. Performance measures reflecting the extent of agreement between guidelines and actually delivered care were defined on the basis of items of the guidelines. An overall performance measure was computed. Additionally, an inventory was made of problems occurring during the implementation of the guidelines. The performance of general practitioners never reached full agreement with the consensus guidelines and it differed between the various performance measures, between the diseases, and between the general practitioners. There is an overall slightly positive trend during the 21-month period, which is reflected in an increase of the performance measure and/or a decrease in the variation between the general practitioners. Increase was particularly noticeable in actions that were to be carried out routinely in the care of patients with hypertension and diabetes mellitus. There was no indication that agreement between guidelines and actual performance was an overall general practitioner characteristic rather than specific for a single disease. Problems mentioned by the general practitioners as underlying cause for discrepancies between guidelines and performance often concerned organizational matters. Peer discussions led to practicable recommendations. It is suggested that guidelines with an immediate impact on the course and management of a disease will be followed more easily than guidelines that only indirectly influence the course of the disease or that aim at risk factors.*

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[*] *Haines A, Feder G. Guidance on guidelines [Editorial]. Br Med J 1992;305:785-786.*

Schellevis FG, Eijk JThM v, Lisdonk EH vd, Velden J vd, Weel C v. Performance of general practitioners in the follow-up care of patients with chronic diseases [Submitted].

6.1. Introduction

Formulating guidelines for optimal care by general practitioners (GPs) is an important step in the process of improving quality of care. Experts do not agree upon whether local or regional groups of GPs should formulate their own guidelines, or central national organizations should perform this task [1-6]. In a recent publication the development of guidelines on various levels (central, local, practice, and individual) was recommended [7]. In The Netherlands central development of guidelines started in 1982 with consensus meetings on controversial issues in specialist care by the 'Centraal Begeleidingsorgaan voor de Intercollegiale Toetsing'. Guidelines ('standards') for optimal GP care are being centrally developed since 1989 by the Dutch College of General Practitioners. In the U.K. the regional model has been adopted [3,4].

The process of formulating guidelines and their implementation in daily practice has so far mostly been evaluated indirectly by interviews with physicians, or by using data on a highly aggregated national level [7-10], rather than directly on the level of individual doctors and their patients [4,11].

This paper reports the evaluation of the implementation of regionally developed guidelines for the follow-up GP care of their patients witch chronic diseases. It is part of a study on the prevalence of chronic morbidity in general practice and on the care delivered to these patients. This project preceded the development of standards by the Dutch College of General Practitioners and the publication of the first standard [12] in anticipation of the increasing number of patients with these diseases in the near future. The implementation of these guidelines in daily practice is evaluated in this article on the following two points:

* whether the actual care of GPs delivered during the follow-up of patients with chronic diseases tends to conform more to consensus guidelines for optimal care in the course of time and what the variation is between GPs and between diseases;
* problems arising during the implementation of these guidelines in daily practice and how these problems are dealt with.

6.2. Methods

Design

An intervention study was carried out during a period of 21 months consisting of three elements: development of guidelines for optimal care, implementation of the guidelines and continuous registration of actually delivered care with follow-up measurements.

Selection of GPs

The selection of practices and GPs has previously been described in detail [13]. In summary, 7 practices (15 GP's) were selected by convenience following their participation in the Dutch National Survey of general practice [14]. The practices were located in the south-east part of the country. The total list size of the practices at the start of the study amounted to 23,534 persons. Two practices were single-handed, four had two GPs and one was a group practice with 5 GPs. Each GP had an own practice list. Three

practices were involved in vocational training for general practice, the others had no special relationship with a university department of general practice.

Selection of patients

Previously, we have described how the GP's identified the patients with at least one of five, most common chronic diseases [13]. For this paper only patients diagnosed before the start of the study and with a complete follow-up under GP care after the start were selected: 613 with hypertension, 95 with diabetes mellitus, 76 with chronic ischaemic heart disease (CIHD), 115 with chronic respiratory disease, and 17 with osteoarthritis of hip and/or knee.

Intervention

Formulation of guidelines

Monthly meetings (except in July and in August) of 60-90 minutes were held with the participating GPs during the entire study period of 21 months, starting in January 1988. These meetings were held in two, sometimes three subgroups. Attendance of all participating GPs was requested. When this was impossible, attendance of at least one representative per practice was urged. The first seven meetings in each subgroup of GPs were aimed at formulating consensus guidelines of optimal follow-up care for each of the five chronic diseases mentioned above. A summary of the 'state of the art' follow-up care and a draft version of proposed guidelines, both produced by the first author, were sent to the participants one week before each meeting. All subgroups received the same material. During the meeting the proposed guidelines were discussed and amended. A written report was prepared of each meeting and discussed and accepted in the next meeting. The presence of the first author at each meeting guaranteed that differences between the subgroups were discussed and that finally identical guidelines were adopted unanimously. Table 6.1 (left column) lists the items of these guidelines for each of the five chronic diseases. All participating GPs explicitly stated their intention to act according to these guidelines and to motivate discrepancies between the guidelines and the actually delivered care.

Implementation of guidelines

During the subsequent meetings the participating GPs received written individual feedback on their actually delivered care. This information was derived from the data registered by the GPs (see further). In each meeting discrepancies between the guidelines and the actual follow-up care for each disease category were discussed using the method of peer review [15]. When discrepancies between the guidelines and the actually delivered care were noted, the GPs were asked what hindered the implementation of the guidelines. Depending on the nature of these problems solutions were sought by clarifying possible resistance against change, by lowering thresholds for changing routines by means of practicable suggestion, or by peer discussion. Again, a written report was made of these meetings, mailed to the participants, discussed and approved at the next meeting.

Registration

Data on actually delivered care were recorded on special forms by the GPs during all consultations with patients during the entire study period. These data included:

- diagnosis made during consultation coded according to the International Classification of Primary Care (ICPC) [16];
- performance of each of the following procedures (Yes/No): physical examination, blood pressure reading, measurement of body weight, blood glucose, serum creatinine, urine albumin excretion, ophthalmological examination (fundoscopy by the GP or referral to the ophthalmologist), influenza vaccination;
- making a follow-up appointment, defined in a term in weeks or months or by a specific date (Yes/No).

Performance measures

For each of the five chronic diseases performance measures were defined, reflecting the extent of agreement of actual performance with performance according to the guidelines for each disease (Table 6.1). The performance measures were computed at first on the patient level and then aggregated to the GP level.

Agreement between performance and guidelines might be an overall GP characteristic rather than be specific for a single disease. This was explored by computing an additional overall measure of agreement per GP. For this purpose the number of diseases for which their performance was rated in the highest tertile class was counted. This overall performance measure reflects the performance of a GP in relation to the performance of the other participating GPs, rather than the degree to which the overall performance of a GP conforms to the guidelines.

Data on problems encountered during the implementation of the guidelines and how these problems were resolved, were derived from the detailed reports of the meetings. These data were interpreted and classified afterwards according to the following categories:
- problems involving organization of the practice;
- problems of motivation;
- lack of specific skill or experience;
- resistance against standardization.

Table 6.1. Guidelines on and measures of performance of general practitioners in the management of five chronic diseases

Guidelines	Performance measures
Hypertension	
* blood pressure measuring at each control visit	* percentage control visits in which blood pressure was measured
* urine albumin measurement once a year	* percentage of hypertensive patients whose urine albumin was measured during the study period
* follow-up appointment after each control visit	* percentage control visits finished by a follow-up appointment

Table 6.1. (continued) Guidelines on and measures of performance of general practitioners in the management of five chronic diseases

Guidelines	Performance measures
Diabetes mellitus	
* taking recent history of signs and symptoms related to diabetes mellitus	-
* blood glucose measurement at each control visit	* percentage control visits in which blood glucose was measured
* body weight measurement at each control visit	* percentage control visits in which body weight was measured
* blood pressure measuring once a year	* percentage of diabetic patients whose blood pressure was measured during the study period
* influenza vaccination once a year	* percentage diabetic patients who were vaccinated against influenza during the study period
* serum creatinine measurement every three years	* percentage diabetic patients whose serum creatinine was measured during the study period
* ophthalmological examination every three years	* percentage diabetic patients who underwent ophthalmological examination during the study period
Chronic ischemic heart disease (CIHD)	
* taking recent history of signs and symptoms due to CIHD	-
* in case of hypertension: blood pressure measurement at each control visit	* percentage CIHD control visits in patients with hypertension in which blood pressure was measured
* in case of obesity: body weight measurement at each control visit	* percentage CIHD control visits in obese patients in which body weight was measured
Chronic respiratory disease (CRD)	
* taking recent history of signs and symptoms due to CRD	-
* lung examination at each control visit	* percentage control visits in which lungs were examined
* influenza vaccination once a year	* percentage CRD patients who were vaccinated against influenza each year
Osteoarthritis hip/knee	
* taking recent history of signs and symptoms due to osteoarthritis	-
* joint examination at each control visit	* percentage control visits in which joint examination took place

Analysis

The entire study period was divided in periods. For patients with diabetes five 4-months periods and for the others three 6-months periods were distinguished according to the guidelines on the frequency of follow-up visits. The performance measures for each disease are presented as medians of the separate follow-up measurements. Interdoctor variation was expressed by the interval between the first and second tertile value. The overall performance measure reflects the frequency per GP of a score in the highest tertile class in the performance in five diseases (range 0-5). Analyses were carried out with SPSS-X and SPSS-PC.

6.3. Results

The mean attendance rate of the individual GPs at the meetings was 68%. When computed on the practice level (attendance of at least one GP per practice) the mean attendance rate was 79%.

Performance measures

Hypertension

Table 6.2 lists the performance measures of the GPs for the follow-up care of patients with hypertension. The GPs conformed increasingly to the guidelines during the study period with a decrease in variation between GPs on the following aspects of care: measuring blood pressure, and making an appointment. This was reflected in a narrowing of the range between the 33-67 percentiles and in the results on the level of individual GPs: 5 GPs had a maximal score on both performance measures in the first period and these remained maximal, measuring blood pressure increased at least 10% in 6 GPs, and making a follow-up appointment increased at least 10% in 5 GPs.
Measurement of albuminuria was rarely performed during the study period (data not shown): once for 60 of the 613 patients and twice or more for eight patients, never in the remaining patients.

Table 6.2. Performance measures of general practitioners (N=15) in patients with hypertension. Median percentages (33- and 67-percentiles) per 6-month period

Mean number of patients per GP: 40.9 (range 1-111)

	Measuring blood pressure		Making appointment	
Period	%	(33-67 percentiles)	%	(33-67 percentiles)
1	90.2	(84.7- 97.0)	83.5	(72.2- 95.7)
2	98.9	(97.1-100.0)	92.6	(90.9- 99.3)
3	99.6	(98.2-100.0)	92.3	(85.1-100.0)

Chronic ischemic heart disease (CIHD)

The performance measures regard only 41 of the 66 CIHD-patients, namely those with hypertension (N=17) and those with obesity (N=24). No clear trend was detectable in measuring blood pressure in hypertensive CIHD patients (mean percentages in period 1, 2 and 3: 100, 75, 80% of the visiting patients) and in measuring body weight in obese patients (27%, 60%, and 50% of the visiting patients, respectively). Aggregation on the GP level resulted in too small, and therefore unreliable, figures.

Diabetes mellitus

Table 6.3 shows the performance of the GPs for patients with diabetes mellitus. The fraction of control visits in which blood glucose was measured increased steadily from 75% to 90% with a decrease in the range between the 33-67 percentiles. The change in performance measures of individual GPs varied: 2 GPs had a maximal score in the first period which remained stable, and 5 GPs showed an increase of at least 10% between the first and the last period. The performance measures of the others remained stable at a lower level or decreased. Measuring body weight was less frequently performed and the increase was marginal: the measure of 2 GPs increased, of another 2 GPs decreased, and the others remained stable. All GPs but one measured the blood pressure of their diabetic patients twice or more during the study period. Only three GPs vaccinated all their diabetic patients against influenza. Serum creatinine was measured during the study period at least once in 24% of the diabetic patients. When extrapolated to three years (according to the guidelines), two GPs would be fully compliant in the measurement of serum creatinine of all their diabetic patients once in three years. Ophthalmological examinations were carried out in 26% of the patients at least once during 21 months. One GP would reach an extrapolated measure of 100% of his diabetics undergoing an ophthalmological examination in three years.

Table 6.3. Performance measures of general practitioners (N=15) in patients with diabetes mellitus. Median percentages (33- and 67-percentiles) per 4-month period

Mean number of patients per GP: 6.3 (range 1-16)

	Measuring glucose		Measuring body weight	
Period	%	(33-67 percentiles)	%	(33-67 percentiles)
1	76.5	(66.7-81.0)	50.5	(31.8-52.8)
2	82.1	(68.8-85.7)	52.1	(30.0-54.2)
3	85.7	(78.6-87.5)	64.3	(35.0-66.7)
4	83.3	(77.1-83.3)	44.4	(12.5-47.2)
5	89.6	(80.0-91.8)	55.0	(25.8-56.3)

Chronic respiratory disease (CRD)

Compliance with the guidelines regarding lung examination remained stable between 80 and 85% during the study period (Table 6.4) with a decrease of the inter-physician variation: 5 GPs remained on their maximum score, and 4 GPs showed an increase of at least 10%. Of the 115 patients 31% were vaccinated against influenza; the vaccination rate per GP ranged from 0 to 60% of the CRD patients.

Table 6.4. Performance measures of general practitioners ($N=15$) in patients with chronic respiratory disease. Median percentages (33- and 67-percentiles) per 6-month period

Mean number of patients per GP: 7.7 (range 1-22)

Period	Lung examination % (33-67 percentiles)
1	92.1 (72.7-100.0)
2	98.6 (75.0-100.0)
3	93.8 (80.0- 95.4)

Osteoarthritis

The agreement of GP performance with the guidelines on the follow-up of osteoarthritis patients, expressed in the fraction of control visits in which joints were examined, decreased during the study period from 72 to 59% (data not shown). These figures are based, however, on limited numbers of patients and control visits. Therefore, aggregation to GP level has not been executed.

Overall measure

The performance of one GP was in the highest percentile of measures for all five diseases (Table 6.5). Three GPs scored below the highest percentile for all five diseases.

Table 6.5. Overall performance of general practitioners ($N=15$) in patients with chronic diseases: frequency of performance score in highest percentile group (range 0-5)

Score	Number of general practitioners
0	3
1	2
2	7
3	2
4	-
5	1

Problems experienced in implementation

The discrepancies between actual performance and guidelines often concerned actions that were to be carried out only intermittently, e.g. once a year, rather than routinely during each follow-up visit. The GPs recognized that it was difficult to implement such a routine in practice. Different solutions were proposed and adopted, e.g. reservation of consultation hours for specific patient groups, or administration by the practice assistant. In general, during the study period all GPs delegated - to a different extent - tasks regarding the follow-up care to the practice assistant, especially for patients with hypertension and diabetes mellitus, assuming that practice assistants would act with more discipline. Making appointments for follow-up visits was increasingly supported by using appointment cards handed out to patients.

The GPs ascribed the interdoctor variation on the performance of intermittent actions to some extent to 'hobbies': high motivation for specific interventions: some GPs were focused on the influenza-vaccination of all patients-at-risk, others were more interested in screening patients for ophthalmological complications, although all GPs agreed on the clinical relevance of these actions.

Lack of experience with certain skills, e.g. fundoscopy or examination of joints, was mentioned as another cause for discrepancy between guidelines and performance. This led in one subgroup to a training by colleagues.

Resistance against standardization of their performance was discovered by discussing individual cases with the GPs in which they considered the guidelines to be useless. Without denying the value of an individualized application of the guidelines we tried to impress during the meetings that inapplicability of guidelines in some cases is not a reason for considering them useless in general.

6.4. Discussion

The performance of GPs never reached full agreement with the consensus guidelines and it differed between the various performance measures, between the diseases, and between the GPs. There is an overall slightly positive trend during the 21-months period, which is reflected in an increase of the performance measure and/or a decrease in the variation between the GPs. The assumption that the degree of agreement between guidelines and actual performance is a general GP characteristic could not be confirmed.

Many and various problems arose during the implementation. During the meetings animated discussions of these problems took place and many creative solutions were proposed. Some of these solutions were implemented in the practices, which can be seen as a positive outcome.

It could be objected that the effects measured in this study can only be validly ascribed to the intervention if a control group of GPs and/or a control period before intervention would have been included. However, it was reasoned that neither approach would have provided a valid control. A control group of GPs would have consisted of physicians who continued to deliver their usual care during the same period without the influence of attending educational programs, reading publications or discussing problems with colleagues on these subjects. This would have created an artificial environment, which does not represent daily general practice anymore. A control group as

well as a 'before and after' design would have included registration of actions during consultations on detailed research forms, without influencing the nature of delivered care. Such registration would undoubtedly have evoked the performance of actions mentioned on the forms, and thus the control group or control period would not have represented the usual care situation. The alternative of collecting information on delivered care from the patients' records would have been unsatisfactory because these are usually restricted to outcome measures relevant for the follow-up of the patients.

Some performance measures showed an increase during the study period, others did not show a clear change. Those that increased reflect actions which had to be carried out routinely and had immediate impact on the further management of the disease: measuring blood pressure in hypertensive patients and blood glucose in diabetic patients. Those that did not change during the study concerned actions that were to be carried out intermittently and/or had to do with risk factors with only potential influence on the disease in the future: vaccination against influenza, measurement of serum creatinine and ophthalmological examination. Apparently, actions with direct consequences for the disease and its management are considered more important and are therefore performed more consistently in the course of time under the influence of the guidelines. This phenomenon requires more attention in research on quality of care and in projects on the implementation of guidelines.

Evaluation of the process of medical care should ideally be carried out by measuring performance of actions which can be considered to be related to the outcome of care. The value of measuring blood pressure in patients with hypertension and blood glucose levels in diabetic patients will not be disputed, but a meaningful performance measure reflecting optimal care for CIHD or osteoarthritis patients is not available. The availability of a meaningful performance measure would be an additional requirement for adequate guidelines [7].

Evaluation of actual GP performance from registered data bears the risk of under- or overestimation of the actual performance. A deficient registration regime is a possible source of underestimation. One could argue, however, that deficient registration represents a low quality of care [17]. Overestimation would occur if the participating GPs registered procedures which they had not actually carried out. This was not checked, but it seems very unlikely that this occurred during the study period, since participation in the study was voluntary, there were no sanctions on non-compliant performance, the atmosphere during the meetings was friendly, and non-compliant performance led to more insight in one's own work.

In this study the actual performance of GPs was compared with the guidelines they had formulated themselves. This has always been a strong point in favour of the regional development of guidelines [7]. The guidelines which the participating GPs agreed upon, reflect minimal optimal care compared to the 'standards' on diabetes mellitus, hypertension, and chronic respiratory disease published subsequently by the Dutch College of General Practitioners [12,18,19]. Thus a performance of 100% compliance with the guidelines would not have been unreasonable. Such full compliance was reached only by some GPs and for some performance items only. We have no clear explanation why this is so, since all GPs participated with enthusiasm until the end of the study. The attendance at the meetings did not decrease during the study period. It has been stated before that "simply feeding back information on performance has almost no impact on changing clinical behaviour" [20]. Feedback most probably

influences clinical practice in doctors who already agreed to review their practice [11]. In this project feedback of information was supported by peer review. More intensive feedback, e.g. on individual cases [21], or a longer implementation period might bring about more changes in performance.

6.5. Conclusions

This paper presents an evaluation of the implementation of guidelines for the follow-up care of patients with chronic diseases. In the course of time, GP performance tended conform more to the guidelines, but 100% agreement was only reached by some GPs on some performance items. Actions which had to be carried out routinely and which had an immediate impact on the management of the disease showed an increasing agreement with the guidelines. Meaningful performance measures were not available for all chronic diseases. Feeding back information on actual performance integrated in a peer review process resulted in practicable recommendations.

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7. Outcome of the follow-up care of patients with chronic diseases by general practitioners

The implementation of consensus guidelines

... Science based on sphygmomanometric readings must not be allowed to overrule the art of personal care ...[*]

Abstract - *The effect of formulating and implementing guidelines for the optimal follow-up care, in combination with registration of delivered care and of outcome was studied longitudinally in patients with chronic diseases in general practice. All patients with hypertension, diabetes mellitus, chronic ischaemic heart disease, chronic respiratory disease, and osteoarthritis of hip and/or knee cared for by 15 general practitioners were identified (N=906 cases) and followed over a period of 21 months. Simultaneously, the general practitioners developed and implemented consensus-based guidelines on the optimal follow-up care for these patients. For each of the five diseases disease status indicators were defined. Patient compliance to follow-up visits and compliance of the general practitioners with the guidelines were the main independent variables. The disease status indicators of the five chronic diseases fluctuated during the study period without showing a substantial change. Trends were found for a relation between patient compliance and increase of normotensive status in hypertensive patients, and between performance of general practitioners and increase of normoglycaemic status of diabetics. No indications were found for an overall, non-disease-related relationship between the compliance of general practitioners with the guidelines for care and change of disease status indicators of the patients. It is argued that the disease status indicators chosen for patients with chronic ischaemic heart disease (normal blood pressure), chronic respiratory disease (number of exacerbations) and osteoarthritis (number of episodes of joint related problems) do not well reflect their disease status. Evaluation of the implementation of guidelines requires the availability of meaningful outcome measures.*

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[*] *Fry J. Common diseases, 4th ed. Lancaster: MTP Press, 1985.*

Schellevis FG, Eijk JThM v, Lisdonk EH vd, Velden J vd, Weel C v. Outcome of the follow-up care of patients with chronic diseases by general practitioners [Submitted].

7.1. Introduction

Our research project aimed at the improvement of quality of care in general practice by implementing guidelines on the follow-up care of patients with chronic diseases. Traditionally, three aspects of quality of care are considered: structure, process and outcome [1]. We were able to study aspects of process and outcome. This study took place within the framework of the Dutch National Survey of General Practice [2], which was aimed, among other things, at gaining insight in the care provided by general practitioners (GPs). In a previous paper we described the care delivered by GPs to patients with common chronic diseases (hypertension, chronic ischemic heart disease, diabetes mellitus, chronic respiratory disease, and osteoarthritis) [3]. This paper reports on the outcome of care.

Outcome of care can be operationalized in different ways, e.g. morbidity, mortality, cost/benefit, subjective and objective health status. We have focused on indicators reflecting the disease status of patients with the above-mentioned chronic diseases:

* What is the effect of the implementation of guidelines for follow-up care on the disease status of patients with chronic diseases in general practice?
* What is the influence of patient characteristics and of compliance of patients and GPs with guidelines?

7.2. Methods

Design

An intervention study was carried out during a period of 21 months, starting 1 January 1988, which consisted of three elements: development of guidelines, implementation of guidelines, and continuous registration of actually delivered care and of disease status indicators of the patients.

Selection of GPs and cases

The selection of GPs and patients has previously been described in detail [3,4]. The GPs identified in their practices all patients known to have one or more of the following diseases:

- hypertension;
- diabetes mellitus;
- chronic ischemic heart disease (CIHD);
- chronic respiratory disease (asthma, chronic bronchitis, emphysema; CRD);
- osteoarthritis of knee and/or hip.

For the purpose of this study the patients had to satisfy the following criteria: diagnosis was made before 1 January 1988, and a complete follow-up GP care during the study period was received.

Intervention

Formulation and implementation of guidelines

As previously described in detail [3], monthly meetings were held during the study period. In the first phase of the study period these meetings were aimed at formulating

guidelines for optimal follow-up care for each of these five chronic diseases. During the last 10 meetings the GPs received individual feedback on their performance as compared with the guidelines. Discrepancies between guidelines and actually provided care were discussed by means of the peer review method.

Registration

During all consultations with the patients data were registered by the GPs on special research forms during the entire study period. These data included items with regard to the actually delivered care, which were used for the feedback meetings [3]. Additionally, data on the disease status of the patients were registered on the same forms. These data included morbidity presented by the patient and results of examinations and laboratory tests.

Measurements

Patient characteristics were measured by the GPs at inclusion and are listed in Table 7.1. Blood pressure was measured by the GPs with a sphygmomanometer or a digital manometer gauged at the start of the study. Diastolic blood pressure was read at the disappearance of the sounds (Korotkoff phase V). Body length was measured once at the start of the study. Body weight was measured at each office with the same balance during the entire study period. Blood glucose levels were generally measured in the office, using blood test strips and a reflectometer, occasionally in a regional laboratory.

Table 7.1. Characteristics of five patient groups with chronic diseases

	Hyper-tension (*N*=613)	Diabetes Mellitus (*N*=95)	CIHD* (*N*=66)	CRD (*N*=115)	Osteo-arthritis (*N*=17)
- Male (%)	31	33	49	58	18
- Age (mean)	60	66	69	49	65
- Initial BP (diastolic - mean - mmHg)	106				
- Baseline BP (diastolic - mean - mmHg)	92		82		
- Baseline BMI (mean - kg/m^2)	28	27			28
- Baseline blood glucose (mean-mmol/l)					
- fasting		8.3			
- non-fasting		10.9			
- Comorbidity (% of *N*)	17	51	45	16	41

* CIHD=chronic ischemic heart disease; CRD=chronic respiratory disease; BP=blood pressure; BMI= body mass index

Diagnoses made during the consultations were coded by trained clerks according to the International Classification of Primary Care (ICPC) [5]. They were clustered into disease episodes ('a problem or illness in a patient over the entire period of time from its onset to its resolution' [6]). At the first consultation of each episode it was indicated whether the episode was 'new' or 'old'.

Measures

Disease status indicators, the dependent variables, were defined for each of the five studied chronic diseases and are listed in Table 7.2. For hypertension, diabetes mellitus, and CIHD these indicators are the same as those mentioned as targets in the guidelines. For CRD and osteoarthritis episodes of exacerbations, acute bronchitis for CRD and joint related problems for osteoarthritis, were chosen as indicators. Body mass index (BMI) was computed using the body weight measured during the consultations and the body length at baseline. Exacerbations of chronic respiratory disease were defined as new episodes of acute bronchitis (ICPC code R78). Joint related problems were defined as new episodes of pain in knee/hip or myalgia (ICPC codes L13, L14, L15, or L18). Incidences were expressed in percentages of patients affected.

Table 7.2. Dependent and independent variables used in the study per chronic disease

	Dependent variables: Disease status indicators	Independent variables: Patient and care characteristics
Hypertension	% of patients with diastolic blood pressure < 95 mmHg	sex age initial blood pressure baseline blood pressure comorbidity patient compliance received care: agreement with guidelines
	% of patients with BMI < 27 kg/m^2	sex age baseline BMI patient compliance
Diabetes mellitus	% of patients with blood glucose fasting < 8.0 mmol/l or non-fasting < 10.0 mmol/l	sex age baseline blood glucose comorbidity patient compliance received care: agreement with guidelines
	% of patients with BMI < 27 kg/m^2	sex age baseline BMI comorbidity patient compliance

Table 7.2. Dependent and independent variables used in the study per chronic disease (continued)

	Dependent variables: Disease status indicators	Independent variables: Patient and care characteristics
Chronic ischemic heart disease	% of patients with diastolic blood pressure < 95 mmHg	sex age baseline blood pressure comorbidity patient compliance
Chronic respiratory disease	incidence of exacerbations	sex age comorbidity
Osteoarthritis	incidence of joint related problems	sex age comorbidity

Patient and care characteristics, the independent variables in this study, are also listed in Table 7.2. Patient characteristics, as age, and diastolic blood pressure and BMI at the start of the study were dichotomised at the median of each disease group separately. Baseline blood glucose was dichotomised at 8.0 mmol/l for the fasting patient status or at 10.0 mmol/l for the non-fasting status. Initial diastolic blood pressure (measured in diagnosing hypertension) was dichotomised at 105 mmHg. As noted previously [7], there were patients with comorbidity. Comorbidity reflects the existence at the start of the study of at least one of the other four chronic diseases. Patient compliance was defined as the attendance at the minimum number of control visits according to the guidelines and dichotomised on the basis of the frequency distribution: 100% compliance vs less than 100%. A variable indicating received follow-up care was computed only for the cases of hypertension and diabetes mellitus, the number of cases in the other disease groups being too small. This variable reflects the agreement between the actual GP performance and the guidelines (observed vs expected) in each case, viz measurement of blood pressure in hypertensive patients and measurement of blood glucose in diabetic patients [3]. This care variable was also dichotomised on the basis of the frequency distribution: 100% agreement vs less than 100%.

Analysis

Analysis of the data was performed per disease. The entire study period was divided in periods. For diabetes five 4-months periods and for the other diseases three 6-months periods were considered according to the guidelines on the frequency of follow-up visits [3]. The disease status indicators are presented as 3 or more follow-up measurements. Subgroups defined by the independent variables were used for subgroup analysis. Analyses were carried out with SPSS-X and SPSS-PC. Confidence intervals (CI) were computed at the 95% level.

7.3. Results

Hypertension

The proportion of hypertensive patients with a diastolic blood pressure below 95 mmHg did not change during the study period (Table 7.3). Sex, age, initial blood pressure, and baseline blood pressure showed no clear influence (data not shown). In 82% of the hypertensive patients the GP measured blood pressure at each control visit, in 18% of the patients it was measured in 0-95% of the control visits. The measurement of the blood pressure by the GP at each control visit had no clear influence on the change in number of normotensive patients (Table 7.3). There was a decreasing trend in the number of normotensive patients in the noncompliant patient group. The number of hypertensive patients with a BMI below 27 kg/m^2 showed an increasing trend in the compliant patient group only (data not shown). In the first and last observation period there were fewer normotensive patients in the comorbidity subgroup than in the non-comorbidity subgroup (Table 7.4).

Table 7.3. Proportion of hypertensive patients with diastolic blood pressure < 95 mmHg during three 6-months periods controlled for GP care and patient compliance

		Received care: agreement with guidelines		Patient compliance	
	Total (N=613)	< 100% (N=78)	100% (N=500)	< 100% (N=183)	100% (N=414)
Period	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
1	74 (70.0-78.0)	76 (63.4-86.4)	74 (69.2-77.8)	79 (69.6-87.1)	73 (68.2-77.2)
2	71 (66.4-74.6)	67 (54.0-78.7)	71 (66.5-75.2)	63 (52.2-73.3)	72 (67.7-76.5)
3	74 (70.2-78.2)	77 (62.5-87.2)	74 (69.5-78.1)	65 (54.1-74.6)	77 (72.2-80.9)

Table 7.4. Proportion of hypertensive patients with diastolic blood pressure < 95 mmHg during three 6-months periods controlled for comorbidity

	Comorbidity	
	Yes (N=107)	No (N=506)
Period	% (95% CI)	% (95% CI)
1	69 (57.6-79.5)	75 (70.6-79.2)
2	71 (58.9-81.0)	70 (66.0-74.8)
3	72 (60.5-81.1)	75 (70.4-79.2)

Diabetes mellitus

The proportion of diabetic patients with a normoglycaemic status fluctuated during the five 4-months periods with a marked dip in the fourth period (Table 7.5). This proportion tended to increase in females, older diabetics, and patients who were hyperglycaemic at baseline (data not shown). In 46% of the diabetic patients the GP measured blood glucose at each control visit. In 54% of the patients blood glucose was measured between 0 and 91% of the control visits. The measurement of blood glucose at each control visit had a positive influence on the number of diabetics with a normoglycaemic status from the second period until the end of the study (Table 7.5).

Table 7.5. Proportion of diabetics with normoglycaemia during five 4-months periods controlled for GP care and patient compliance

		Received care: agreement with guidelines		Patient compliance	
	Total (N=95)	< 100% (N=50)	100% (N=44)	< 100% (N=39)	100% (N=55)
Period	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
1	47 (34.3-59.8)	61 (43.4-76.0)	27 (11.6-47.8)	40 (16.3-67.7)	49 (34.4-63.7)
2	44 (30.9-58.6)	39 (21.5-59.4)	50 (29.9-70.1)	39 (13.9-68.4)	46 (30.7-62.6)
3	49 (35.6-62.7)	47 (28.3-65.7)	52 (32.0-71.3)	53 (26.6-78.7)	48 (32.0-63.6)
4	32 (20.3-45.0)	22 (8.6-42.3)	39 (22.9-57.9)	29 (10.3-56.0)	33 (19.1-48.5)
5	47 (33.6-61.2)	39 (20.2-59.4)	55 (35.7-73.6)	53 (26.6-78.7)	45 (29.3-61.5)

Patient compliance in follow-up visits did not seem to influence the proportion of diabetics with normoglycaemia over time. Normoglycaemia tended to be more common in diabetics with comorbidity than in those without comorbidity, although the fluctuations over time in both subgroups were considerable (Table 7.6). The number of diabetics with a BMI < 27 kg/m^2 fluctuated around 50%. These figures were not clearly influenced by sex, age, BMI at baseline or patient compliance (data not shown).

Table 7.6. Proportion of diabetics with normoglycaemia during five 4-months periods controlled for comorbidity

	Comorbidity	
	Yes (*N*=48)	No (*N*=47)
Period	% (95% CI)	% (95% CI)
1	56 (37.9-72.8)	37 (19.9-56.1)
2	40 (21.1-61.3)	48 (29.4-67.5)
3	52 (32.5-70.6)	46 (27.5-66.1)
4	36 (19.2-54.6)	28 (12.7-47.2)
5	50 (29.9-70.1)	45 (26.4-64.3)

Chronic ischemic heart disease

The majority of CIHD patients in this study had already a diastolic blood pressure below 95 mmHg at baseline. Their number increased during the study period (Table 7.7). Subgroup analysis revealed an increasing trend in women and older patients, and in the subgroup with a higher diastolic blood pressure at baseline, but comorbidity had no influence on these results (data not shown). The results in the small number of compliant patients do not allow any conclusion.

Table 7.7. Proportion of CIHD patients with diastolic blood pressure < 95 mmHg during three 6-months periods controlled for patient compliance

		Patient compliance	
	Total (*N*=66)	< 100% (*N*=57)	100% (*N*=6)
Period	% (95%CI)	% (95% CI)	% (95% CI)
1	87 (71.2-95.3)	84 (66.3-94.5)	100 (54.1-100.0)
2	91 (77.9-97.4)	89 (74.6-97.0)	100 (54.1-100.0)
3	91 (77.9-97.4)	89 (74.6-97.0)	100 (54.1-100.0)

Chronic respiratory disease

The overall incidence of exacerbations in patients with CRD did not change during the study period (Table 7.8). Analyses of subgroups showed an increased incidence in the older patients. Comorbidity did not seem to influence the incidence of exacerbations over time.

Table 7.8. Incidence of exacerbations in CRD patients during three 6-months periods controlled for comorbidity in percentages

		Comorbidity	
	Total (N=115)	Yes (N=18)	No (N=97)
Period	% (95% CI)	% (95% CI)	% (95% CI)
1	19 (11.9-26.3)	22 (6.4-47.6)	19 (11.4-27.7)
2	22 (14.2-29.3)	33 (13.3-59.0)	20 (12.2-28.9)
3	17 (9.7-23.3)	17 (3.6-41.4)	17 (9.7-25.4)

Osteoarthritis

The 17 patients with osteoarthritis presented three new episodes of joint complaints to their GPs, one in the second semester and two in the last six months. These incidence rates did not allow any further analysis of subgroups.

7.4. Discussion

The development and implementation of guidelines were aimed at improving the quality of care. Improvement of doctor's compliance with guidelines and of patient compliance with follow-up visits is generally expected to improve the outcome in patients [8], but there is little empirical evidence to support this. Therefore, this study was exploring the relation between performance and outcome. Ideally, such an intervention study should include a control group and/or baseline data collected in the period before intervention. For reasons previously explained [3], no such controlled design was adopted.

In this study the disease status indicators of patients with five common chronic diseases fluctuated during the study period without a clear change. The results indicate improvement in some patient groups:

- non-compliant hypertensive patients decrease with regards to their normotensive status;
- in diabetic patients care according to guidelines increases the normoglycaemic status over time.

More detailed analysis of patients whose disease status indicators improved and whose did not could reveal patient or care characteristics that facilitated the effects. The findings here are only trends, as the confidence intervals show much overlap. Patient compliance and received care could only be adequately studied for patients with hypertension and with diabetes mellitus for whom a simple quantitative measure could be computed. Similar trends might be visible in other patient groups if such measures would be available. Our results for diabetic patients are in accordance with a recent report on the influence of patient, doctor, practice and care characteristics on control in

diabetes mellitus, where only 15% of the variation of glycolysated haemoglobin between patients could be explained [9]. In another study participation by GPs in standard setting for common childhood conditions showed improved respiratory function in their patients [10]. We know of no other published studies in which outcome of care was related to patient compliance and GP performance.

The disease status indicators used in this paper are those upon which GPs usually base their management in daily practice. They reflect 'short-term' results as in the case of diastolic blood pressure and blood glucose. For CIHD patients, however, diastolic blood pressure does not really reflect their disease status, but there is no obvious alternative short-term indicator. The disease status of patients with CRD could be reflected by peak flow or spirometric measures. A proposal to include routine measurement of peak flow could not reach consensus approval of the participating GPs. In the 'standard' of the Dutch College of General Practitioners, that was published afterwards, routine peak flow measurement is included [11]. For patients with osteoarthritis no adequate numerical disease status indicator is available. Taking episodes of joint related problems as an indicator, just as exacerbations in CRD patients, was therefore a poor man's choice. For chronic diseases only long-term outcome measures as cardiovascular morbidity or mortality, diabetic retinopathy, respiratory function are really meaningful. Including, however, these measures in an intervention study requires a far longer study period.

There could be an interaction between patient compliance and delivered care since delivery of optimal care is only possible in fully compliant patients. This interaction was not taken into account in our study. As none of the univariate analyses showed significant differences it did not seem meaningful to carry out multivariate analysis.

Taking into account five chronic diseases simultaneously implies a broad approach rather than a study in detail. One could assume that GP performance is not related to a single disease but a general GP characteristic. We did not find any indication for this assumption in the data on GP performance [3], or in the data shown here: there was no relation between overall GP performance and outcome expressed in the proportion of patients who kept stable or improved on the disease status indicators.

Apparently, the relation between delivered and received care and outcome is more complex than is generally expected. Further study should focus on measures representing elements of care that are considered essential. In addition, more attention is needed to indicators that reflect the course of a chronic disease, to be used in research as well as in daily care.

7.5. Conclusions

The development and implementation of guidelines for the follow-up care of patients with chronic diseases may have a positive effect on the short-term disease status indicators. In this study only some positive trends were found and some influence of received care and patient compliance. Measuring the outcome of GP care for patients with chronic diseases requires the availability of meaningful quantitative disease status indicators. To elucidate the influence of GP compliance with guidelines for optimal care, of patient compliance, and of their interaction will require further study.

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8. Discussion

The study reported in this thesis is a part of the Dutch National Survey of General Practice, which is aimed at gaining insight into the patterns of diseases presented in general practice and the care provided by general practitioners (GPs). This part of the survey focused on chronic diseases with special attention to comorbidity and quality of care. In this last chapter conclusions are formulated, and methodological issues and the relevance of this study for investigators and general practitioners are discussed.

8.1. Conclusions

The following conclusions are formulated for the research questions mentioned in chapter 1.

a. How can comorbidity be defined?

From a systematic search of the relevant literature we concluded that there is no uniformity in defining comorbidity or in the diseases that are considered in studying comorbidity. We proposed a definition and classification based on the presumed relationship between diseases.

b. What is the validity of diagnoses of chronic diseases in general practice?

Diagnoses registered on patient records in general practice can be considered largely valid, since in our study of the records of 15 GPs we found only small proportions of false positive diagnoses (less than 4%).

c. What is the prevalence of comorbidity of chronic diseases?

The point-prevalent concurrence of the five most common chronic diseases in general practice (hypertension, diabetes mellitus, chronic ischaemic heart disease, chronic respiratory disease, and osteoarthritis of knee and/or hip) had a high prevalence in patients with at least one of these diseases, especially in patients of 65 years and older. The highest rates of comorbidity were found in patients of 65 and over with diabetes mellitus, and with osteoarthritis.

d. What is the influence of comorbidity of chronic diseases on GP consultation rates and on the incidences of intercurrent diseases?

Consultation rates in general practice tended to be higher for patients with comorbidity than for patients with only one of the five chronic diseases, and compared with patients without any chronic disease. Patients with comorbidity of chronic diseases tended to have higher incidence rates of intercurrent morbidity than patients without comorbidity.

e. *Does the actual care of GPs during the follow-up of patients with chronic diseases become more in agreement with the consensus guidelines for optimal care in course of time?*

The actually delivered care by general practitioners did not come to full agreement with the guidelines in the course of time. However, agreement tended to increase with time, particularly in the care for patients with hypertension and diabetes mellitus concerning actions that had to be carried out at each visit.

f. *What is the effect of the implementation of guidelines for follow-up care on the disease status of patients with chronic diseases in general practice?*

The disease status of the five chronic diseases studied fluctuated during the study period without showing a substantial change. Trends were found for a relation between patient compliance and increase of normotensive status in hypertensive patients, and between performance of general practitioners and increase of normoglycaemic status of diabetic patients.

8.2. Methodological aspects

In performing research in general practice one meets many and complex problems which need to be dealt with. Four of these are discussed here: diagnostic validity, the prevalence of comorbidity, the analysis of the influence of comorbidity on consultation rates and morbidity, and the use of a control group and/or a control period.

The validity of diagnoses of chronic diseases was established by measuring the true positive and false positive diagnoses. The picture of validity is, however, not complete without measuring true negative and false negative diagnoses. This would require a screening procedure in (a sample of) the practice population for five chronic diseases which was not feasible within this study.

The prevalence of comorbidity of chronic diseases depends greatly on the number of diseases that is considered. Although the chronic diseases included in this study are responsible for the majority of chronic morbidity in general practice, the presented figures of comorbidity are strictly valid only within the scope of these five chronic diseases.

The influence of comorbidity on consultation rates and intercurrent morbidity was difficult to measure. Results are at risk of being biased by patient age, and possibly by other diseases present on which no information is available. Many diseases are age-dependent or aging-related. In studying a specific disease the influence of age can be controlled for methodologically. In the case of a chronic disease it is difficult to disentangle the influence of age and of the disease itself. In the case of comorbidity this is even more complex. Another problem is the overlap between the different co-morbidity subgroups: patients with diabetes mellitus and hypertension appear in both the comorbidity subgroup of hypertensive patients and diabetic patients.

The effect of guidelines on actual care and patient outcome is also difficult to establish. The use of a control group or of measurements prior to the intervention are methodologically recommended, or sometimes even considered obligatory. However, it

appears virtually to have a true control group or baseline period. GPs in a control group cannot be asked to continue their usual care without taking notice of medical literature or educational programs during the study period. In the case of a baseline measurement the registration of activities on the same form that is used during the intervention period will undoubtedly influence the GPs in their performance in the direction of the intervention. These considerations concern the general question whether it is advisable to strive for the creation of a laboratory-like situation in general practice studies especially in view of the generalizability of the results. In our study we have, after careful consideration, decided not to do this, although we realize that this limits the internal validity of our study.

8.3. Relevance for investigators

The revival of attention for the phenomenon of comorbidity of chronic diseases is a good opportunity to combine efforts of investigators in order to reach more uniformity in definition, operationalization and use of comorbidity in epidemiological and clinical studies. A first step should include the explicit mentioning of definitions and of diseases considered. A further step should be the development of a classification of comorbidity, of a measure of comorbidity, and uniform handling of comorbidity in epidemiological and clinical studies. We suggested a classification based on the type of relationship between diseases: concurrent, cluster, causal, and complicating comorbidity. This classification needs further validation. Finally, the relevance of comorbidity should be brought to the attention of investigators, especially of those who study chronic diseases. The relevance for daily practice of such studies is enhanced when comorbidity is taken into account. Therefore, further descriptive studies should be undertaken in order to gain more insight into comorbidity and its relation to age, sex, and other patient characteristics. Comorbidity presents a real challenge for epidemiological and clinical research.

General practice in The Netherlands harbours a resource of morbidity and mortality data which is largely underestimated. Internationally, Dutch general practice is almost unique in its fixed practice list. This offers the possibility of computing epidemiological denominators and the completeness and validity of morbidity data, depending of course on the GP's accuracy. This unique position will be further enhanced by the increasing use of computerized information systems in the near future. This should lead to a wider use of general practices for descriptive studies and also as a sampling frame for case control and intervention studies.

Until now, the structure, process, and outcome of care have mostly been studied independently from each other. Measures of delivered care were not related to data on outcome in patients who received that care. The implementation of guidelines has so far mostly been evaluated at the level of institutions or even at a national level. In our view, the implementation of guidelines should be accompanied by feedback at the level of individual GPs and sometimes even at the level of individual patients. The requirement for GPs to register their performance provides a secondary, but nevertheless important benefit in that it makes them more aware of their performance. The formulation and implementation of guidelines, and registration of performance permit studies of the quality of GP care: information on GP performance is easily available at the level of the individual patient. When this information is linked with outcome

measures, obtained either by the GP or by extra data collection from patients, quality of care studies become possible. The performance measures should be disease-specific, underwritten by GPs as considered useful, and should be related to meaningful outcome measures. The disease-specific outcome measures should provide either insight into the short term course of the disease or information on prognostic factors that are generally considered relevant for the specific disease. Studies on quality of care should not only focus on disease-specific outcome parameters but also on the functional health status in its broadest sense. The relation between performance and outcome is not that simple as could be expected, especially in the comprehensive care of patients with chronic diseases. It is difficult to define performance measures that reflect important elements of the care process. Measuring real outcome in patients with chronic diseases requires longitudinal studies in which many other interventions than the doctor's performance may occur.

8.4. Relevance for general practitioners

The objective of this study was to contribute to the knowledge about chronic diseases in general practice. The results present a kaleidoscopic view of this field. This study illustrates and emphasizes the very important position of GPs in the care of patients with chronic diseases. Chronic diseases are diagnosed mostly by GPs and the validity of their diagnoses is confirmed in this study. Comorbidity of chronic diseases is a quantitatively important phenomenon in patients over 65 years old and it will increase in the near future. These patients consult their GP frequently, mainly for acute intercurrent diseases. Consequently, GPs are confronted with multiple health problems which may pose difficult problems. The GP has the most complete overview of all these problems and is in the best position to manage these complex situations. Patients with comorbidity appeal strongly to the generalistic nature of a GP's work. This important position of GPs in The Netherlands should be elaborated and GPs should profit from it in maintaining and reinforcing their position in the health care system for patients with chronic diseases. The recognition of comorbidity as an important feature of general practice should have consequences for the single-disease standards of the Dutch College of General Practitioners.

The formulation and implementation of guidelines in general practice, aimed at improving the quality of care of patients with chronic diseases is an intensive job. The agreement between the guidelines and actual performance in this study was already high at the beginning with regard to some measures and did therefore not change appreciably during the implementation. In other measures trends in the positive direction were found. There is a need for further discussion on the relevance of detailed performance measures, on whether full agreement between guidelines and performance in all patients should be pursued, and on whether less than 100% agreement between guidelines and performance reflects qualitatively inferior care. One of the main objectives of the Dutch standards is improving the outcome in patients by optimal GP performance. Eventually, standards should list only those performance items which have proven to be effective on outcome parameters.

In this study a simple model of peer review was used. More intensive feedback on actually delivered care in combination with educational programs focusing on deter-

mined needs might have more success. Such a diversity of methods should be built into quality improvement programs for general practitioners. There were no significant effects of GP performance on the disease status of patients with chronic diseases in this study, so no conclusions can be drawn from this part. The last two chapters of this thesis present a model for the evaluation of care which can be used in peer review groups, and in vocational training. In this way GPs can evaluate systematically their performance in delivering care and its effects on patients.

9. Summary

The study reported in this thesis is a part of the Dutch National Survey of General Practice, which is aimed at gaining insight in the patterns of diseases presented in general practice and in the care provided by general practitioners (GPs). This part of the survey focuses on chronic diseases with special attention to comorbidity and quality of care.

Chapter 1 gives background information on the main themes of this study, and lists the questions which this study aims to answer. It also provides some information on the setting of general practice in The Netherlands. The prevalence of chronic diseases is expected to increase in the near future due to the 'greying' of the population over the next decades. Care for patients with chronic diseases is mainly aimed at the compression of disabling lifetime. Comorbidity of chronic diseases, the existence of more than one chronic disease in one patient, has until recently not received much attention. Yet it is a reality of the daily practice of GPs who have to deal with all diseases of a patient. The following five chronic diseases were chosen for this study: hypertension, chronic ischaemic heart disease, diabetes mellitus, chronic respiratory disease, and osteoarthritis of knee and/or hip.

Chapter 2 reports the results of a search of the literature aimed at clarifying differences in defining and handling the phenomenon of comorbidity in order to contribute to greater uniformity. A systematic MedLine search using the key word 'comorbidity' yielded 70 publications between 1985 and 1991. A review of these publications revealed that comorbidity was defined explicitly in 33 publications. These definitions rested upon the type of relationship between diseases: co-existence of diseases, presence of diseases additional to an index disease, and association or correlation between diseases. Diseases that were considered in studying comorbidity were mostly of a chronic nature (diabetes mellitus, cancer, heart disease). In the reviewed publications comorbidity was most frequently used as an independent variable. Comorbidity was handled differently, varying from a simple measure reflecting the presence or absence of any comorbid disease to complex comorbidity measures weighted for disease severity. Mortality or survival was the most frequently studied outcome variable. It was concluded that for a better understanding of the role of comorbidity there is a need for an agreed definition, for explicit mentioning of the diseases considered, and for standardization of measures of comorbidity.

In *chapter 3* a study of the validity of diagnoses of chronic diseases is reported. The certainty of a diagnosis of a chronic disease is most important for the patient but also for morbidity studies. The certainty of a diagnosis was operationalized by measuring the agreement with diagnostic criteria according to the International Classification of Health Problems in Primary Care. Data on the performance and results of diagnostic procedures were collected retrospectively by 15 GPs in seven general practices. The agreement with the diagnostic criteria for the diseases diagnosed in general practice was high, ranging from 96% true positive cases in diabetes mellitus to 58% in chronic respiratory disease. The highest rate of false positive cases was 4%. The variation between the 15 GPs in the agreement of the diagnoses of their patients with the diagnostic criteria was substantial. It was concluded that the diagnoses of the five

diseases registered in general practice are generally valid with low numbers of false positive cases.

The extent of comorbidity of five chronic diseases which were in agreement with diagnostic criteria is described in *chapter 4*. In the population under 65 years of age comorbidity occurred in only 0.3%. In persons of 65 years and older 23% suffered from one or more of the diseases studied. Within this patient group 15% suffered from more than one of the diseases. Patients with osteoarthritis, and with diabetes mellitus had the highest rates of comorbidity. Comorbidity is thus a clinical reality of general practice.

The influence of comorbidity of chronic diseases on the frequency of consultations of GPs and on intercurrent morbidity is described in *chapter 5*. For this purpose the number of consultations and the incidence rates of intercurrent morbidity were studied during 21 months in five cohorts of patients grouped according to their chronic disease. Within each cohort a distinction was made between patients with one and patients with two or more of the five studied diseases. In each cohort patients with comorbidity had higher consultation rates than single-disease patients. Intercurrent diseases were presented more frequently to the GP by patients with comorbidity than single-disease patients. Most intercurrent morbidity consisted of acute common diseases as myalgia, upper respiratory tract infection and urinary tract infection. Compared to reference groups without any chronic disease, single-disease patients had higher consultation rates but no higher incidence rates of intercurrent morbidity.

Chapter 6 describes a study on the effect of formulating and implementing guidelines for optimal follow-up care of patients with chronic diseases on actually delivered care. In monthly meetings with the 15 participating GPs consensus was reached on guidelines, followed by their implementation in daily practice. The implementation was supported by feeding back information on actual performance integrated in peer review meetings. At the same time the GPs registered data on the care delivered to their patients during 21 months. The agreement between guidelines and actually delivered care to five groups of patients was expressed in performance measures per disease. An overall performance measure was computed. Additionally, an inventory was made of problems occurring during the implementation of these guidelines. The performance did not reach full agreement with the guidelines, but agreement tended to increase in the course of time. This was particularly noticeable in the performance towards patients with hypertension, and with diabetes mellitus with regard to actions that had to be carried out at each visit. There was no indication that agreement between guidelines and actual performance is an overall GP characteristic, rather than specific for a single disease. Problems mentioned by the GPs as underlying cause for discrepancies between guidelines and performance frequently concerned organizational matters. Peer discussions led to practicable suggestions. It was argued that the formulation and implementation of guidelines will improve more easily performance with an immediate impact on the course and management of a disease than performance with only an indirect influence on the course of a disease.

Chapter 7 describes a study on the effect of guidelines for optimal follow up care on patient outcome measures. During the implementation of these guidelines the GPs not only registered data on the actually delivered care, as analyzed in chapter 6, but also the results of measurements and presented morbidity. For all five chronic diseases outcome measures reflecting the disease status were defined. Patient compliance to follow-up visits, and GP performance according to the guidelines were used as indepen-

dent variables. The disease status indicators of the five patient groups fluctuated during the study period of 21 months without showing a substantial change. Trends were found for a relation between patient compliance and increase of normotensive status in hypertensive patients, and between performance of GPs and increase of normoglycaemic status of diabetics. No indications were found for an overall, non-disease-related relationship between the compliance of GPs towards care according to the guidelines and change of disease indicators of their patients. It was concluded that the outcome measures for patients with chronic ischaemic heart disease (normal blood pressure), chronic respiratory disease (number of exacerbations), and osteoarthritis (number of episodes of joint related problems) do not well reflect their disease status. Evaluation of the implementation of guidelines requires the availability of meaningful performance and outcome measures.

In *chapter 8* conclusions are formulated, and methodological issues and the relevance of this study for investigators and general practitioners are discussed. Studies on the effects of comorbidity are at risk of being biased by, for example, age. This can be controlled for methodologically, but the relevance of studying a net effect of comorbidity for daily medical practice can be doubted. It is suggested that the application of methodologically ideal models reduces the external validity of the results of studies of the delivery of care and its effects on patients. For epidemiological and clinical investigators the issue of comorbidity presents a real challenge. It is recommended to pursue more uniformity in defining and handling comorbidity in research, and studies on the relation with age, sex, and other patient characteristics. The almost unique source of morbidity and mortality data in the Dutch general practices deserves further use. Further development of research on quality of care, with simultaneous measurement of performance and outcome, is indicated. The functional health status of patients should be incorporated in measuring outcome. For general practitioners this study confirms their important position in the care for patients with chronic diseases. Patients with comorbidity of chronic diseases appeal strongly to the generalistic nature of a GP's work. Therefore comorbidity should be systematically included in the Dutch standards for optimal GP care. Programs aimed at improving quality of care should include diverse strategies. The relevance of pursuing full agreement between guidelines and actually delivered care should be discussed. The model presented in this study can well be used in educational programs focusing on the implementation of a systematic evaluation of the effects of delivered care in general practice.

Samenvatting

In deze dissertatie wordt een deelonderzoek beschreven van de Nationale Studie naar Ziekten en Verrichtingen in de Huisartspraktijk. De Nationale Studie had tot doel inzicht te verkrijgen in de presentatie van ziekten, klachten en problemen in de huisartspraktijk en in de door huisartsen naar aanleiding hiervan ondernomen acties. Chronische ziekten en in het bijzonder comorbiditeit en kwaliteit van zorg zijn onderwerp van dit deelonderzoek van de Nationale Studie.

In *hoofdstuk 1* vindt men achtergrondinformatie over de thema's van het onderzoek en de onderzoeksvragen. De positie van de huisarts in het Nederlandse gezondheidszorgsysteem wordt kort toegelicht. De prevalentie van chronische ziekten zal naar verwachting in de naaste toekomst toenemen door de 'vergrijzing' van de bevolking. De zorg voor patiënten met chronische ziekten is vooral gericht op de vermindering van het aantal jaren met beperkingen. Aan comorbiditeit, het vóórkomen van meer dan een ziekte bij dezelfde patiënt, is nog weinig aandacht besteed. Comorbiditeit behoort tot de realiteit van de dagelijkse praktijk van de huisarts die met alle ziekten van een patiënt rekening moet houden. Voor dit onderzoek zijn vijf chronische ziekten gekozen: hypertensie, chronische ischemische hartziekten, diabetes mellitus, chronische aspecifieke respiratoire aandoeningen en gonartrose en/of coxartrose.

In *hoofdstuk 2* wordt een literatuuronderzoek beschreven naar de verschillen in definities van comorbiditeit en de plaats van comorbiditeit in onderzoeken. Het doel van dit literatuuronderzoek was een bijdrage te leveren aan een grotere uniformiteit. Systematisch zoeken met behulp van MedLine leverde 70 publicaties op uit de jaren 1985-1991. In 33 publicaties werd comorbiditeit expliciet gedefinieerd. Deze definities bleken gebaseerd op de aard van de relatie tussen ziekten: het tegelijkertijd vóórkomen van ziekten, de aanwezigheid van een andere ziekte dan de bestudeerde of 'index-ziekte' en associatie of correlatie tussen ziekten. De ziekten die in beschouwing werden genomen bij het bestuderen van comorbiditeit waren meestal van chronische aard (diabetes mellitus, kanker, hartziekte). In de bestudeerde publicaties fungeerde comorbiditeit meestal als onafhankelijke variabele. De wijze waarop comorbiditeit in de analyse van de gegevens werd gebruikt varieerde van eenvoudigweg de aan- of afwezigheid van enige andere ziekte tot gecompliceerde maten voor comorbiditeit met weging voor de ernst van ziekten. De meest gebruikte uitkomstvariabele was sterfte of overleving. De conclusies van dit literatuuronderzoek zijn dat er behoefte is aan een algemeen onderschreven definitie, aan het expliciet vermelden van de ziekten die in beschouwing worden genomen en aan standaardisatie van maten voor comorbiditeit.

In *hoofdstuk 3* wordt verslag gedaan van een onderzoek naar de validiteit van de gestelde diagnoses van chronische ziekten. Zekerheid over de diagnose is belangrijk voor patiënten, maar ook voor studies naar frequenties van ziekten. De zekerheid over de diagnose werd afgemeten aan de mate waarin werd voldaan aan de diagnostische criteria volgens de 'International Classification of Health Problems in Primary Care'. Retrospectief verzamelden 15 huisartsen in zeven huisartspraktijken gegevens over diagnostische handelingen en resultaten van diagnostisch onderzoek. De overeenkomst met de diagnostische criteria varieerde van 96% terecht positieve diagnoses diabetes mellitus tot 58% van de patiënten met chronische aspecifieke respiratoire aandoenin-

gen. Het hoogste percentage fout-positieve diagnoses was 4. De 15 huisartsen verschilden onderling sterk wat betreft het voldoen van de door hen gestelde diagnoses aan de diagnostische criteria. De conclusie van dit onderzoek luidt dat de diagnoses van de vijf chronische ziekten, geregistreerd in de huisartspraktijk, in het algemeen valide zijn met lage aantallen fout-positieve diagnoses.

De omvang van comorbiditeit bij vijf chronische ziekten voor zover deze voldeden aan de diagnostische criteria wordt beschreven in *hoofdstuk 4*. In de bevolking jonger dan 65 jaar kwam comorbiditeit maar bij 0,3% van de mensen voor. Bij personen boven 65 jaar was 23% bekend met tenminste een van de vijf chronische ziekten. Van deze laatsten heeft 15% meer dan één chronische ziekte. Comorbiditeit kwam het meest frequent voor bij patiënten met artrose en met diabetes mellitus. Comorbiditeit is dus realiteit in de huisartspraktijk.

De invloed van comorbiditeit van chronische ziekten op de frequentie van contacten met de huisarts en op het optreden van andere ziekten wordt beschreven in *hoofdstuk 5*. Gedurende 21 maanden werd het aantal contacten en het aantal nieuw optredende ziekten bepaald uitgaande van elke van de vijf chronische ziekten. Binnen iedere groep werd onderscheid gemaakt tussen patiënten met één of meer van de vijf ziekten. Deze laatsten zijn de patiënten met comorbiditeit. Binnen alle groepen hadden de patiënten met comorbiditeit een hogere contactfrequentie dan de patiënten met één chronische ziekte. Ook presenteerden de patiënten met comorbiditeit meer nieuwe ziekten aan de huisarts dan de patiënten met één chronische ziekte. Myalgie, bovenste-luchtweginfectie en urineweginfectie waren de meest frequente nieuwe ziekten. In vergelijking met referentiegroepen zonder chronische ziekte hadden patiënten met uitsluitend hypertensie en patiënten met uitsluitend diabetes mellitus een hogere contactfrequentie, maar presenteerden zij niet meer nieuwe ziekten.

In *hoofdstuk 6* wordt verslag gedaan van een onderzoek naar effecten van het opstellen en invoeren van richtlijnen voor optimale lange-termijnzorg op de daadwerkelijk verleende zorg aan patiënten met chronische ziekten. Tijdens maandelijkse bijeenkomsten stelden de 15 deelnemende huisartsen, op basis van consensus, richtlijnen op en voerden deze in in de dagelijkse praktijk. De invoering van de richtlijnen werd ondersteund door gegevens over het feitelijk handelen terug te koppelen aan de huisartsen en deze informatie te bespreken met behulp van de methode van onderlinge toetsing. De huisartsen registreerden gedurende 21 maanden gegevens over de door hen verleende zorg. Per ziekte werden maten geconstrueerd voor overeenstemming tussen de richtlijnen en het feitelijk handelen. Ook werd een totaalmaat geconstrueerd voor het handelen van de huisarts. Daarnaast werden de problemen die rezen tijdens de invoering van de richtlijnen geïnventariseerd. Er werd geen volledige overeenstemming tussen de richtlijnen en het feitelijk handelen bereikt. Wel was er in de loop van de tijd een toenemende mate van overeenstemming. Dit was vooral duidelijk voor handelingen die, in geval van hypertensie en diabetes mellitus, tijdens elk contact uitgevoerd dienden te worden. De mate van overeenkomst tussen de richtlijnen en het feitelijk handelen bleek geen algemeen kenmerk van huisartsen in plaats van een ziekte-gebonden huisartskenmerk. De problemen die door de huisartsen werden genoemd als verklaring voor het ontbreken van de overeenstemming tussen de richtlijnen en het handelen waren vaak van organisatorische aard. De discussies daarover tijdens de bijeenkomsten leverden praktisch toepasbare adviezen op. Er wordt betoogd dat het opstellen en invoeren van richtlijnen eerder een positieve invloed heeft op handelingen die direct

gerelateerd zijn aan het beloop van de ziekte dan op handelingen die indirect verband daarmee houden.

In *hoofdstuk 7* wordt een onderzoek beschreven over effecten van de invoering van richtlijnen voor optimale lange-termijnzorg op het ziektebeloop bij patiënten. Tijdens de invoering van deze richtlijnen registreerden de deelnemende huisartsen niet alleen gegevens over hun feitelijk handelen (zie hoofdstuk 6), maar ook de resultaten in maat en getal en gepresenteerde ziekten. Voor ieder van de vijf chronische ziekten werden klinische uitkomstmaten geconstrueerd als indicatoren voor het beloop van de ziekte. De bezoektrouw van patiënten en de mate waarin het feitelijk handelen van de huisarts overeenkomt met de richtlijnen waren de onafhankelijke variabelen. De indicatoren voor het beloop van de ziekte schommelden gedurende de onderzoeksperiode zonder duidelijk te veranderen. Er lijkt verband te bestaan tussen bezoektrouw van patiënten en een toename van het aantal goed ingestelde hypertensiepatiënten, en tussen het handelen van de huisarts en een toename van het aantal goed ingestelde diabetespatiënten. Er waren geen aanwijzingen voor een algemeen, niet-ziektegebonden, verband tussen het handelen van huisartsen volgens de richtlijnen en veranderingen in de ziekte-indicatoren van hun patiënten. De conclusie is dat de gekozen uitkomstmaten voor patiënten met een chronische ischemische hartziekte (normotensie), chronische aspecifieke respiratoire aandoeningen (aantal exacerbaties) en artrose (aantal episoden gewrichtsproblemen) het ziektebeloop niet goed weergeven. Om de invoering van richtlijnen te kunnen evalueren moeten zinvolle uitkomstmaten beschikbaar zijn.

In *hoofdstuk 8* worden conclusies geformuleerd en methodologische aspecten bediscussieerd. Ook wordt de betekenis van dit onderzoek voor onderzoekers en voor huisartsen besproken. Onderzoek naar effecten van comorbiditeit worden potentieel verstoord door bijvoorbeeld leeftijd. Hoewel hiervoor methodologisch gecorrigeerd kan worden, kan men zich afvragen wat de relevantie is voor de dagelijkse praktijk van het bestuderen van het 'netto' effect van comorbiditeit. Een methodologisch ideale onderzoeksopzet bij onderzoek naar verleende zorg en de effecten daarvan op patiënten vermindert de externe validiteit van de gevonden resultaten. Voor epidemiologisch en klinisch onderzoek vormt het verschijnsel comorbiditeit een echte uitdaging. Aanbevolen wordt om meer uniformiteit na te streven in de definitie en het gebruik van comorbiditeit , en om de relatie tussen comorbiditeit en leeftijd, geslacht en andere patiëntkenmerken nader uit te diepen. Huisartspraktijken in Nederland vormen daartoe een vrijwel unieke lokatie gezien de beschikbaarheid van gegevens over ziekte en sterfte. Onderzoek naar kwaliteit van zorg, met het gelijktijdig meten van handelen en uitkomsten, dient verder te worden ontwikkeld. Als uitkomstmaat is de functionele gezondheid van patiënten hierbij goed bruikbaar. Dit onderzoek bevestigt de belangrijke positie van de huisarts in de zorg voor patiënten met chronische ziekten. De zorg voor patiënten met comorbiditeit appelleert sterk aan het generalistische karakter van het werk van de huisarts. Comorbiditeit zou een vaste plaats moeten krijgen in de standaarden van het Nederlands Huisartsen Genootschap. Programma's die gericht zijn op verbetering van de kwaliteit van zorg dienen verschillende methoden te omvatten. Besproken moet worden wat het belang is van volledige overeenstemming tussen richtlijnen en het feitelijk handelen van huisartsen. Het model dat in dit onderzoek gebruikt is, is geschikt voor scholingsprogramma's die zijn gericht op het systematisch evalueren van de effecten van de verleende huisartsgeneeskundige zorg.

Résumé

L'étude rapportée dans cette thèse est une contribution à l'Enquête Nationale néerlandaise sur la Médecine Générale entreprise pour préciser la nature des affections rencontrées par les omnipraticiens ainsi que les sanctions thérapeutiques qu'ils leur opposent. Cette partie de l'enquête porte sur les maladies chroniques et plus particulièrement sur les polypathologies et la qualité des thérapeutiques mises en oeuvre.

Le *Chapitre 1* situe les principaux volets de cette étude et énumère les questions auxquelles elle ambitionne de répondre. Il renseigne également sur l'organisation de la médecine générale aux Pays-Bas. On peut tabler sur une augmentation de la prévalence des maladies chroniques dans les prochaines décades. Le traitement des maladies chroniques vise essentiellement à repousser l'échéance de l'état d'impotence. Les états polypathologiques chroniques, c'est-à-dire de coexistence de plus d'une affection chronique chez le même malade, n'ont guère retenu l'attention jusqu'à présent. Ces situations sont pourtant le lot quotidien des généralistes qui ont à gérer l'ensemble des pathologies présentées par leurs patients. Pour cette étude ont été retenues les cinq affections chroniques suivantes: hypertension permanente, ischémie myocardique chronique, diabète sucré, affections respiratoires chroniques, arthrose du genou et/ou de la hanche.

Le *Chapitre 2* rapporte les résultats des recherches bibliographiques entreprises pour faire le point sur les différentes acceptions et utilisations du concept de polypathologie et contribuer ainsi à une meilleure uniformisation de la terminologie. Une recherche MedLine systématique à partir du mot clé 'polypathologie' aboutit à la sélection de 70 publications parues entre 1985 et 1991. Leur examen révéla que la définition du terme 'polypathologie' était explicite dans 33 d'entre elles. Les définitions se fondaient sur la nature des relations entre différentes affections: coexistence de pathologies différentes, existence de pathologies surajoutées à une affection principale et associations ou corrélations entre plusieurs pathologies. Les maladies prises en considération pour l'étude de polypathologies étaient pour la majorité d'entre elles de nature chronique (diabète sucré, cancers, cardiopathies). Dans toutes ces publications, la polypathologie était le plus souvent considérée comme une variable indépendante. Le terme de polypathologie recouvrait des significations différentes, allant de la simple appréciation de l'existence ou non d'une maladie concomitante jusqu'à la notion complexe d'appréciation d'un degré de gravité. L'intérêt se portait le plus souvent sur le taux de mortalité ou les chances de survie. On peut conclure de ces recherches que, pour une meilleure compréhension des phénomènes liés aux états de polypathologies, il est nécessaire de trouver un consensus sur la définition de ce terme, de préciser la nature des maladies prises en considération et de standardiser les paramètres d'évaluation de ces états.

Le *Chapitre 3* est consacré à l'étude de la validité des diagnostics posés en matière de maladies chroniques. Si la fiabilité d'un diagnostic est d'importance capitale pour le patient, elle l'est aussi pour celui qui étudie la morbidité. La validité des diagnostics a été appréciée en se référant aux critères retenus pour la Classification Internationale des Problèmes de Santé pour les Soins Primaires. Les données sur les démarches diagnostiques et leurs résultats furent recueillis de façon rétrospective auprès de quinze

omnipraticiens exerçant dans sept cabinets médicaux. La concordance avec les critères diagnostiques fut trouvée très bonne, allant de 96% de vrais positifs pour le diabète sucré à 58% pour les affections respiratoires chroniques. Le taux de faux positifs le plus élevé était de 4%. De nettes différences de concordance entre diagnostics posés et critères diagnostiques furent observées d'un praticien á l'autre. En définitive, on peut dire que, pour ce qui est des cinq maladies choisies pour cette étude, les diagnostics posés en médecine générale sont généralement corrects avec peu de faux positifs.

Le *Chapitre 4* traite de l'importance de la polypathologie afférente aux cinq affections chroniques étudiées, satisfaisant aux critères diagnostiques. Cette polypathologie ne touche que 0,3% de la population de moins de 65 ans. Parmi les gens âgés de 65 ans et plus, on compte 23% de personnes atteintes d'une ou plusieurs des maladies étudiées. Dans ce groupe de patients, 15% présentent plus d'une maladie. Les personnes souffrant d'arthrose et de diabète sucré sont les plus nombreuses à présenter une polypathologie qui se trouve donc être en effet une entité clinique rencontrée en médecine générale.

L'influence des états de polypathologie d'affections chroniques sur le taux de fréquentation des cabinets des omnipraticiens et sur la fréquence des maladies intercurrentes est analysée dans le *Chapitre 5*. Pour ce faire, ces deux paramètres ont été colligés sur une période de 21 mois, pour cinq cohortes de malades répartis selon la nature de leurs affections chroniques. Pour chacune de ces cohortes, la distinction était faite entre patients à pathologie unique et patients porteurs de deux ou plus des cinq affections en cause. Dans tous les cas, on a constaté que les malades à polypathologie consultaient plus souvent que ceux qui ne souffrent que d'une seule affection. De même, la fréquence d'apparition de maladies intercurrentes était majorée pour les malades à polypathologie. Ces maladies intercurrentes étaient généralement des épisodes aigus d'affections banales, telles que myalgie, infections des voies respiratoires supérieures et de la sphère urinaire. D'autre part, par rapport aux groupes témoins, sans pathologie chronique, on relevait bien une majoration du nombre de consultations, mais sans modification de l'incidence de maladies intercurrentes.

Le *Chapitre 6* est consacré à l'étude de l'impact sur la pratique journalière des directives thérapeutiques formulées et mises en oeuvre pour optimiser le suivi médical de malades chroniques. Des réunions mensuelles avec les quinze généralistes engagés dans l'étude ont abouti à un consensus sur des directives et leur mise en application dans la pratique journalière. Cette mise en application était appuyée par les retours d'expérience commentés lors de réunions critiques. Pendant toute cette période de 21 mois, les praticiens enregistraient des données sur les soins prodigués à leurs patients. La concordance entre les directives et les soins réellement dispensés aux cinq groupes de malades était exprimée par évaluation de résultats pour chacune des maladies. Une évaluation globale était menée parallèlement. Accesoirement, on dressa l'inventaire des difficultés apparues dans l'application de ces directives. La concordance entre pratique et directives ne fut pas totale, mais on constate son amélioration au fil du temps. Cela fut particulièrement patent pour le suivi de patients hypertendus et diabétiques en ce qui concernait le contenu de chaque visite. Rien ne permettait de dire que la concordance entre directives et pratique réelle était pour ces généralistes le fait d'une tendance générale plutôt qu'un fait lié à une maladie précise. Les difficultés mentionnées par les médecins comme responsables de défaut de compliance aux directives étaient fréquemment d'ordre matériel et liées à des questions d'organisation. Les

discussions entre participants à l'enquête ont été fécondes en suggestions. Il apparaît que la mise au point et l'utilisation de directives généraient une compliance meilleure quand l'impact était immédiat sur le cours de la maladie et sa prise en charge et que celle-ci laissait à désirer en cas de retombée indirecte sur le cours des choses.

Le *Chapitre 7* est consacrè à l'analyse des résultats obtenus par l'application des directives pour l'optimisation du suivi médical. Pendant la durée de cette application, les praticiens ne se contentèrent pas de noter quels étaient les soins réellement pratiqués, ainsi qu'il a été dit au chapitre 6, mais ils relevèrent également les paramètres biologiques recherchés ainsi que la pathologie constatée. Ces differents paramètres témoins de l'affection furent définis pour les cinq maladies étudiées. La compliance des patients aux visites de suivi, d'une part, et l'observance des directives par les praticiens, d'autre part, ont été traitées comme des variables indépendantes. Les marqueurs de la pathologie des cinq groupes de patients fluctuèrent tout au long des 21 mois que dura l'observation, mais sans grand changement. On observa une tendance à la normalisation des chiffres tensionnels liée à la compliance du patient hypertendu ainsi qu'une tendance à la normalisation des taux de glycémie du patient diabétique liée aux prestations des médecins. Aucun indice n'a été trouvé en faveur de l'existence d'un lien d'ordre général et non lié à l'état pathologique entre la compliance des généralistes aux procédures de soins définies dans les directives et des modifications des marqueurs des pathologies de leurs patients. On conclut que les paramètres biologiques des patients atteints d'ischémie du myocarde (chiffres tensionnels normaux), d'affection respiratoire chronique (nombre de poussées) et d'arthrose (nombre d'accès articulaires) ne reflètent pas fidèlement leur état pathologique. L'évaluation de la méthode des directives thérapeutiques nécessite d'avoir à sa disposition des résultats cliniques et biologiques significatifs.

Le *Chapitre 8* est celui des conclusions. On y discute de questions de méthodologie et de l'intérêt de ce travail pour des chercheurs et des omnipraticiens. L'étude des polypathologies risque d'être biaisée par le facteur âge par exemple. Si l'on peut neutraliser méthodologiquement les effets de cette variable, on peut par contre avoir des doutes sur la pertinence d'une étude de l'impact net de la polypathologie pour la pratique journalière. Il semble que la mise en oeuvre de modèles méthodologiquement parfaits se traduise par une diminution de la validité externe des résultats des enquêtes sur les soins médicaux prodigués et leurs effets sur les patients. Pour les chercheurs, tant épidémiologistes que cliniciens, les problèmes posés par les polypathologies sont un vrai défi. Il faudrait arriver à davantage de rigueur dans la définition et l'utilisation de la notion de polypathologie en recherche médicale ainsi que dans l'étude des facteurs âge, sexe et autres paramètres liés aux patients. L'unique, ou presque unique, source de données sur la morbidité et la mortalité en pratique de médecine générale aux Pays-Bas mérite donc d'être exploitée davantage. L'élargissement de la recherche sur la qualité des soins avec évaluation de la pratique et des résultats est donc indiquée. Il devrait être tenu compte de l'état fonctionnel des patients dans cette évaluation. Le rôle des médecins généralistes dans le suivi de patients atteints de maladies chroniques se trouve confirmé par cette étude. Les malades souffrant de polypathologies relèvent forcément de leur compétence. C'est la raison pour laquelle les situations de polypathologies devraient être systématiquement incluses dans les 'protocols' de soins optimums à l'usage des acteurs de la médecine générale aux Pays-Bas. Les programmes visant à améliorer la qualité des soins devraient être diversifiés. Le bien-fondé de recherche

d'une concordance absolue entre les directives de soins et la pratique courante devrait être discuté. La présente étude peut très bien servir de support à des formations en matière d'évaluation de résultats pour la médecine générale.

Zusammenfassung

Die Studie, die in dieser Dissertation dargestellt wird, ist Teil der Nationalen Niederländischen Untersuchung in Allgemeinpraxen, die das Ziel hat, Einblick in die Erkrankungsformen und deren Versorgung durch den Allgemeinarzt zu geben. Dieser Teil der Studie befaßt sich schwerpunktmäßig mit chronischen Erkrankungen, insbesondere ihrer Komorbidität und der Qualität der Versorgung.

Kapitel 1 erläutert den Hintergrund der Hauptthemen dieser Studie und stellt Fragen zusammen, die die Studie beantworten möchte. Es liefert auch einige Informationen über die Bedeutung der Allgemeinmedizin in den Niederlanden. Es wird erwartet, daß die Prävalenz von chronischen Erkrankungen in der nahen Zukunft aufgrund der 'Überalterung' der Bevölkerung während der nächsten Jahrzehnte ansteigt. Die Hauptaufgabe bei der Betreuung von Patienten mit chronischen Erkrankungen ist es, den Zeitraum mit hohem Leidensdruck zu verkürzen. Der Komorbidität bei chronischen Erkrankungen, dem Vorhandensein von mehr als einer chronifizierten Erkrankung bei einem Patienten, galt bis vor kurzem wenig Aufmerksamkeit. Tatsächlich betreut aber der Allgemeinarzt alle Erkrankungen eines Patienten in der täglichen Arbeit. Für diese Studie sind die folgenden fünf Erkrankungen ausgewählt worden: Bluthochdruck, chronische ischämische Herzkrankheit, Diabetes mellitus, chronische Erkrankungen der Atemwege und Osteoarthritis in Knie und/oder Hüfte.

Kapitel 2 faßt die Ergebnisse einer Literaturrecherche zusammen. Ziel der Recherche war, Unterschiede in der Definition und dem Umgang mit dem Begriff Komorbidität aufzudecken, um einen Beitrag zur Vereinheitlichung zu leisten. Eine systematische MedLine Recherche mit dem Schlagwort 'Komorbidität' lieferte 70 Publikationen für den Zeitraum zwischen 1985 und 1991. Eine Analyse dieser Publikationen machte deutlich, daß Komorbidität in 33 Publikationen ausdrücklich definiert worden ist. Diese Definitionen reflektierten die Beziehungen zwischen den Einzelerkrankungen: die Koexistenz von Erkrankungen, das Vorhandensein von Erkrankungen zusätzlich zu einer Index-Erkrankung sowie Nähe und Korrelationen zwischen Erkrankungen. Die Erkrankungen, die untersucht worden sind um Komorbidität zu studieren, waren meist chronischer Art (Diabetes mellitus, Krebs-, Herzerkrankungen). In den untersuchten Publikationen ist Komorbidität am meisten als unabhängige Variable angesehen worden. Die Auffaßung von Komorbidität reichte von einer einfachen Darstellung in Form von dem Vorhandensein bzw. Nicht-Vorhandensein einer komorbiden Erkrankung bis hin zur komplexen Darstellung von Komorbidität als gewichtete Schwere einer Erkrankung. Mortalität oder Überleben war die am häufigsten untersuchte Ergebnis-Variable. Es ist festgestellt worden, daß für ein besseres Verständnis der Bedeutung der Komorbidität die Notwendigkeit einer einheitlichen Definition, einer ausdrücklichen Darstellung der betrachteten Erkrankung und einer Standardisierung bei den Meßgrößen der Komorbidität besteht.

In *Kapitel 3* wird eine Untersuchung der Validität der Diagnosen von chronischen Erkrankungen dargestellt. Die Sicherheit mit der eine chronische Erkrankung diagnostiziert wird, ist für den Patienten am wichtigsten, sie ist aber ebenso bedeutsam für Morbiditätsstudien. Die Sicherheit einer Diagnosestellung ist operationalisiert worden, indem die Übereinstimmung mit den diagnostischen Kriterien analog der Internationa-

len Klassifikation von Gesundheitsproblemen in der Allgemeinpraxis gemessen worden ist. Daten über die Durchführung und Resultate von diagnostischen Maßnahmen sind retrospektiv durch 15 Allgemeinärzte in sieben Allgemeinpraxen gesammelt worden. Die Übereinstimmung mit den diagnostischen Kriterien für die diagnostizierten Erkrankungen war hoch, sie reichte von 96% richtig positiven Fällen bei Diabetes mellitus bis zu 58% bei chronischen Erkrankungen der Atemwege. Die höchste Rate von falsch positiven Fällen war 4%. Die Unterschiede zwischen den 15 Allgemeinärzten hinsichtlich der Übereinstimmung bei den Diagnosen ihrer Patienten mit den diagnostischen Kriterien waren auffällig. Es ist die Schlußfolgerung gezogen worden, daß die Diagnosen der fünf in Allgemeinpraxen registrierten Erkrankungen im allgemeinen valide sind mit einer geringen Anzahl von falsch positiven Fällen.

Das Ausmaß der Komorbidität der fünf chronischen Erkrankungen hinsichtlich der Übereinstimmung mit den diagnostischen Kriterien ist in *Kapitel 4* beschrieben. In der Bevölkerungsgruppe unter 65 Jahren kommt die Komorbidität nur zu 0.3% vor. Personen über 65 Jahren und älter leiden zu 23% an einer oder mehreren der untersuchten Erkrankungen. In dieser Patientengruppe leiden 15% an mehr als einer dieser Erkrankungen. Patienten mit Osteoarthritis und mit Diabetes mellitus haben die höchste Komorbiditätsrate. Komorbidität ist demnach eine klinische Realität der Allgemeinpraxis.

Der Einfluß der Komorbidität von chronischen Erkrankungen auf die Häufigkeit der Konsultation eines Allgemeinarztes und auf eine zusätzlich auftretende Erkrankung ist in *Kapitel 5* beschrieben. Zu diesem Zweck ist die Anzahl der Konsultationen und die Inzidenz dazukommender Morbidität für die Dauer von 21 Monaten in fünf Kohorten von Patientengruppen entsprechend ihren chronischen Erkrankungen untersucht worden. Innerhalb jeder Kohorte ist zwischen Patienten mit einer solchen Erkrankung und Patienten mit zwei und mehr der fünf untersuchten Erkrankungen unterschieden worden. In jeder Kohorte weisen Patienten mit Komorbidität höhere Konsultationsraten auf als Patienten mit einer Erkrankung. Zusätzlich auftauchende Erkrankungen sind dem Allgemeinarzt häufiger von Patienten mit Komorbidität als von Patienten mit einer Erkrankung präsentiert worden. Die häufigsten Erkrankungen, die zusätzlich aufgetreten sind, waren akute Erkrankungen wie Myalgien, Infektionen der oberen Atemwege und urologische Infektionen. Im Vergleich zur Kontrollgruppe ohne chronische Erkrankung, wiesen Patienten mit einer Erkrankung höhere Konsultationsraten, aber kein höhere Inzidenz von zusätzlich auftretende Erkrankungen auf.

Kapitel 6 beschreibt eine Studie über die Auswirkungen der Erstellung und Implementierung von Richtlinien für optimale Nachsorge von Patienten mit chronischen Erkrankungen auf die tatsächlich durchgeführte Behandlung. In monatlichen Treffen von 15 teilnehmende Allgemeinärzte ist Konsens erreicht worden über Richtlinien, gefolgt von ihrer Implementierung in der täglichen Praxis. Die Implementierung ist dadurch unterstützt worden, daß in Expertenrunden über die tatsächlich vorgenommenen Maßnahmen Feedback gegeben worden ist. Zur selben Zeit haben die Allgemeinärzte Daten über die Behandlung gesammelt, die sie innerhalb von 21 Monaten an ihren Patienten durchgeführt haben. Die Übereinstimmung zwischen den Richtlinien und der tatsächlich durchgeführten Versorgung der 5 verschiedenen Patientengruppen wurde mit Hilfe von durchgeführten Maßnahmen pro Erkrankung vorgestellt. Es ist über alle Gruppen eine Messung der Maßnahmen ermittelt worden. Zusätzlich ist eine Bestandsaufnahme über die Probleme gemacht worden, die während der Implementie-

rung dieser Richtlinien aufgetreten sind. Die Ausführungen haben keine volle Übereinstimmung mit den Richtlinien erreicht, aber die Übereinstimmung schien im Laufe der Zeit zu wachsen. Dies war besonders auffällig bei der Anwendung der Richtlinien bei Patienten mit Bluthochdruck und Diabetes mellitus im Hinblick auf Untersuchungen, die bei jedem Praxisbesuch durchgeführt werden müssen. Es gab keinen Anhaltspunkt dafür, daß die Übereinstimmung zwischen Richtlinien und tatsächlichen Leistungen ein generelles Charakteristikum der Allgemeinarzt noch spezifisch für eine Einzelerkrankung ist. Probleme, die von den Allgemeinärzte als Begründung für die Diskrepanzen zwischen den Richtlinien und den Ausführungen erwähnt werden, betreffen meistens organisatorische Gründe. Diskussionen im Expertenkreis führten zu praktikablen Vorschlägen. Es wurde diskutiert, daß die Erstellung und Einführung von Richtlinien eher zu verbessern ist, wenn die Benutzung dieser Richtlinien einen direkten Einfluß auf Verlauf und Behandlung einer Erkrankung hat und schwieriger erscheint, wenn die Durchführung den Krankheitsverlauf nur indirekt beeinflußt.

Kapitel 7 beschreibt eine Untersuchung über die Auswirkungen der Richtlinien auf die optimale Nachsorge von Patienten-Ergebnis-Messungen. Während der Implementierung dieser Richtlinien haben die Allgemeinärzte nicht nur Daten über die tatsächlich durchgeführte Behandlung gesammelt, wie in Kapitel 6 analysiert, sondern darüber hinaus die Ergebnisse der Messungen und der präsentierten Morbidität. Für alle fünf chronischen Erkrankungen sind Ergebnis-Messungen definiert worden, die den Zustand der Erkrankung beschreiben. Die Compliance der Patienten hinsichtlich der Folgekonsultationen und die Ausführungen des Allgemeinarztes analog zu den Richtlinien sind als unabhängige Variablen gesetzt worden. Die Indikatoren für den Erkrankungszustand der fünf Patientengruppen fluktuierten während des Untersuchungszeitraums von 21 Monaten, ohne wesentliche Änderungen zu zeigen. Hinweise auf einen Zusammenhang zwischen der Patientencompliance und einer Annäherung an einen normotensiven Status bei Bluthochdruckpatienten und zwischen den Ausführungen des Allgemeinarztes und der Zunahme von normoglycämischem Status bei Diabetiker konnten gefunden werden. Es sind keine Hinweise gefunden worden für einen generellen, nicht-krankheitsbezogenen Zusammenhang zwischen der Compliance der Allgemeinärzte hinsichtlich der Versorgung analog der Richtlinien und Krankheitsveränderungen ihrer Patienten. Es ist die Schlußfolgerung gezogen worden, daß die Ergebnis-Messungen für Patienten mit chronischen ischämischen Herzerkrankungen (normotensiver Blutdruck), chronischen Erkrankungen der Atemwege (Anzahl der Anfälle) und Osteoarthritis (Anzahl der Episoden von Gelenkproblemen) den Krankheitszustand nicht gut wiedergeben. Die Evaluation der Einführung der Richtlinien verlangt die Verfügbarkeit von sinnvollen Maßnahmen- und Ergebnis-Messungen.

In *Kapitel 8* werden Schlußfolgerungen formuliert sowie methodische Ziele und die Bedeutung dieser Untersuchung für Forscher und Allgemeinärzte diskutiert. Studien über die Auswirkungen der Komorbidität sind in Gefahr den Einfluß von z.B. Alter zu betrachten. Dies kann methodisch kontrolliert werden, aber die Relevanz einer Untersuchung über die netto Auswirkung von Komorbidität für die täglichen medizinische Praxis kann bezweifelt werden. Es wird suggeriert, daß die Anwendung methodisch idealer Modelle die externe Validität von Studienergebnissen, die sich auf Versorgung und deren Auswirkungen für den Patienten beziehen, reduziert. Für epidemiologische und klinische Forscher stellt das Thema der Komorbidität eine echte Herausforderung dar. Es wird vorgeschlagen, eine größere Einheitlichkeit bei der Definition und

Handhabung von Komorbidität in der Forschung und in Studien über den Zusammenhang mit Alter, Geschlecht und anderen Patientencharakteristika anzustreben. Die nahezu einzige Quelle von Morbiditäts- und Mortalitätsdaten in Niederländischen Allgemeinpraxen verdient weitere Anwendung. Die Weiterentwicklung der Forschungen über die Qualität der Versorgung, mit gleichzeitiger Messung der Maßnahmen und der Ergebnisse, ist notwendig. Der funktionale Gesundheitszustand von Patienten sollte bei der Messung der Ergebnisse mit einbezogen werden. Für Allgemeinärzte unterstreicht die Studie ihre bedeutende Rolle in der Versorgung von Patienten mit chronischen Erkrankungen. Patienten mit Komorbidität von chronischen Erkrankungen fordern die umfaßende Betreuung durch Allgemeinärtze. Aus diesem Grund sollte Komorbidität systematisch in die Niederländischen 'Standards' für eine optimale Versorgung integriert werden. Programme mit der Zielsetzung, die Qualität der Versorgung zu verbessern, sollten unterschiedliche Strategien umfassen. Die Relevanz der vollen Übereinstimmung zwischen Richtlinien und aktueller Versorgung in der ärztlichen Praxis sollte diskutiert werden. Das vorgestellte Modell dieser Studie könnte durchaus für Ausbildungsprogramme benutzt werden, die auf die Implementierung einer systematischen Evaluation der Effekte von durchgeführter Versorgung in der Allgemeinpraxis abzielen.

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I dedicate this thesis to my parents - they guided me, they gave me the opportunity for studying medicine, they always supported me in going my way in life and they still do.

Meike and Jebbe: well, this is the book!

Curriculum vitae

François Georges Schellevis, the author of this thesis, was born as the oldest child of a French mother and a Dutch father on February 9, 1953 in Biezelinge (province of Zeeland), 10 days after the flood disaster in that region. He finished primary school in Gouda and obtained his Gymnasium-ß certificate in 1971 at the Christelijk Lyceum in Arnhem. Medical education took place at the Faculty of Medicine of the University of Nijmegen, finished by graduation as MD in 1979. After his vocational training at the Department of General Practice of the University of Nijmegen and in the practice of Karel Sorgedrager in Terborg, he settled in 1982 as a part-time general practitioner in a rural area in the province of Noord-Brabant, together with his partner Marion Bonting.

During his medical education he participated for several years in curriculum evaluation studies. Between 1982 and 1988 he was involved with research and development projects at the Department of General Practice of the University of Nijmegen, concerning registration and classification of medical data in general practice, audit and peer review by general practitioners, and the subject of this thesis.

In 1989 he was appointed full-time staff member at the Department of General Practice and Nursing Home Medicine / Institute for Research in Extramural Medicine of the Vrije Universiteit Amsterdam. He participates in several research projects as an investigator and tutor, and in the management of ongoing research.

He lives in Driebergen with Marion and their two children Meike (born in 1984) and Jebbe (1987).

Appendix

Methodological aspects of 70 publications on comorbidity (chapter 2)

Ref #	Design	Place comorbidity	Measure *	Index disease/ condition	Main outcome variable(s)
5	cross-sect	conf/modif	N of dis	arthritis	disability
6	cross-sect	conf/modif	com Y/N	arthritis	earnings losses
7	cross-sect	outcome var	N of dis spec dis Y/N	-	comorbidity
8	cross-sect	outcome var	spec dis Y/N	diabetes mellitus	comorbidity
9	cross-sect	conf/modif	com Y/N	arthritis	a. disability b. earnings loss
10	cross-sect	outcome var	spec dis Y/N	epilepsy	comorbidity
11	longitudinal	outcome var	com Y/N	cancer on death certificate	trends in cause of death
12	cross-sect	conf/modif	N of dis	arthritis	disability
13	cross-sect	indep var	N of dis	arthritis	disability
14	cohort	indep var	com Y/N	chronic pain	response to epidural electrical stimulation
15	cross-sect	outcome var	spec dis Y/N	multiple sclerosis	comorbidity
16	cohort	indep var	spec dis Y/N	rheumatoid arthritis	mortality
17	Delphi-process	indep var	index	gastrointestinal diseases	appropriateness of procedures
18	cohort	outcome var	spec dis Y/N	recurrent spontaneous abortion	comorbidity

* N of dis: number (sum) of diseases; com Y/N: comorbity present or absent (one variable); spec dis Y/N: specific diseases separately present or absent (multiple variables).

Ref #	Design	Place comorbidity	Measure *	Index disease/ condition	Main outcome variable(s)
19	cross-sect	indep var	N of dis com Y/N	rheumatoid arthritis	a. correlation with index disease and depression b. functional status and demand for care
20	cohort	outcome var	spec dis Y/N	chronic urticaria	comorbidity
21	case-control	outcome var	spec dis Y/N	lichen planus	comorbidity
22	case-control	outcome var	spec dis Y/N	essential tremor migraine headache	comorbidity
23	cohort	conf/modif	index	cognitive impairment	in-hospital morbidity and mortality
24	validation study	indep var ('golden standard')	index	hospital admission	accuracy of estimation of illness severity
25	cohort	indep var	com Y/N	hospital admission	a. preference for intervention type b. in-hospital course
26	cohort	conf/modif	N of dis	stroke	disability and use of services
27	cohort	conf/modif	spec dis Y/N	diabetic hyperosmolar state	mortality
28	cohort	conf/modif	index	breast cancer	pattern of care
29	validation study	variable to be validated	index	hospital admission	accuracy of prediction of mortality
30	validation study	one of the variables to be validated	com Y/N	hospital admission	use of health care after hospital admission
31	cohort	indep var	com Y/N	cancer	complications and mortality

Ref #	Design	Place comorbidity	Measure	Index disease/ condition	Main outcome variable(s)
32	cross-sect	conf/modif	index	cancer	hospital mortality rates
33	cohort	indep var	N of dis	myocardial infarction	outcome at discharge
34	validation study	one of the variables to be validated	N of prescriptions	cataract	visual acuity
35	cohort	indep var	index	hospital admission	one-year survival
36	cohort	indep var	index	lupus nephritis	renal failure and mortality
37	validation study	one of the variables to be validated	N of dis index	prostatectomy cholecystectomy bypass surgery	readmission and mortality
38	cohort	indep var	spec dis Y/N	cardiac surgery	mortality
39	longitudinal	outcome var	spec dis Y/N	cardiac reoperation	trends in patient characteristics and mortality rates
40	validation study	one of the variables to be validated	com Y/N	blood culture	result of blood culture
41	cohort	indep var	spec dis Y/N	hypertension diabetes mellitus	intraoperative hypotension or hypertension
42	cohort	indep var	spec dis Y/N	anaesthesia	mortality
43	case-control	indep var	N of dis spec dis Y/N	trauma	mortality
44	cohort	a. indep var b. conf/modif	spec dis Y/N	coronary heart disease	a. disability b. differences between sexes
45	case-control	indep var	spec dis Y/N	sternotomy	infection and mortality
46	cohort	indep var	com Y/N	non-Hodgkin lymphoma	morbidity and mortality

Ref #	Design	Place comorbidity	Measure	Index disease/ condition	Main outcome variable(s)
47	cohort	indep var	spec dis Y/N	cecal pseudo-obstruction	treatment type
48	reliability study	comparison variable	spec dis Y/N	prostatectomy cholecystectomy	agreement between two data sources
49	cohort	indep var	spec dis Y/N	lower limb amputation	walking ability
50	cohort	indep var	spec dis Y/N	benign prostatic hyperplasia	perioperative complications
51	cohort	conf/modif	index	bypass surgery	hospital and surgeon mortality rates
52	validation study	one of the variables to be validated	N of dis	hospital admission	hospital mortality rates
53	cohort	a. indep var b. conf/modif	index	acute myocardial infarction, bypass surgery, total hip replacement, chole-cystectomy	a. hospital means of length of stay b. mortality, functional status, readmission, patient statis-faction
54	review	conf/modif	spec dis Y/N	scleroderma	mortality
55	cohort	indep var	spec dis Y/N	rheumatoid arthritis	length of stay
56-64	*not included in review*				
65	cross-sect	outcome var	spec dis Y/N	hypertension	comorbidity
66	cross-sect	indep var	N of dis spec dis Y/N	-	disability
67	cohort	indep var	N of dis	-	a. mortality b. incident morbidity c. occurrence of depression
68	cohort	conf/modif	N of dis	rheumatoid arthritis	health outcome

Ref #	Design	Place comorbidity	Measure *	Index disease/ condition	Main outcome variable(s)
69	cross-sect	conf/modif	spec dis Y/N	arthritis	wage earnings
70	cross-sect	conf/modif	N of dis	rheumatoid arthritis	treatment
71	longitudinal	conf/modif	spec dis Y/N	acute myocardial infarction	case fatality rate and survival
72	cross-sect	conf/modif	N of dis	bypass surgery, aneurysm resection, gastrectomy, colectomy, cholecystectomy	mortality for ranges of hospital and surgeon volume
73	cross-sect	conf/modif	index	17 conditions	mortality
74	cross-sect	conf/modif	com Y/N	16 conditions	length of stay and mortality
75	cohort	conf/modif	index	intensive care admission	mortality
76	cohort	indep var	a. spec dis Y/N b. com Y/N	endometrial cancer	survival
77	cross-sect	conf/modif	N of dis	cerebrovascular accident, myocardial infarction, pneumonia	hospital mortality rates
78	cohort	conf/modif	com Y/N	benign prostatic hypertrophy	mortality rates, reoperation rates
79	cohort	outcome var	spec dis Y/N	admission geriatric unit	comorbidity
80	validation study	variable to be validated	spec dis Y/N	diabetes mellitus	accuracy of prediction of death and occurrence of complications
81	cross-sect	indep var	N of dis	-	disability
	cohort	indep var	spec dis Y/N	-	a. decline of functioning b. mortality
	cohort	indep var	spec dis Y/N	-	admission long term and/or mortality

Ref #	Design	Place comorbidity	Measure *	Index disease/ condition	Main outcome variable(s)
82	cohort	indep var	spec dis Y/N	-	longevity
83	cohort	outcome var	spec dis Y/N	diabetes mellitus	comorbidity

Stellingen

1. De huisarts is de 'controlerend geneesheer' bij uitstek voor patiënten met comorbiditeit van chronische ziekten.

2. Epidemiologisch onderzoek naar comorbiditeit vereist het analyseren van ziekten op patiëntniveau.

3. In NHG-standaarden dient bij chronische ziekten standaard aandacht besteed te worden aan comorbiditeit.

4. Iemand met een chronische ziekte is lang niet altijd chronisch ziek.

5. *Les patients patients n'ont que rarement besoin d'un médecin.*

6. Artsen onderschatten zelfzorg.

7. Helpen is niet hetzelfde als aan de hulpvraag beantwoorden.

8. Geneeskunst vereist kunde.

9. Het routinematig vaccineren van jongens tegen rubella is overbodig medisch handelen.

10. Specialisten zijn er dankzij het bestaan van generalisten en niet andersom.

11. Begeleiding van een onderzoeker betekent ook scholing van de begeleider.

12. De vermelding 'Deze ruimte alleen gebruiken voor doeleinden waarvoor deze is bestemd Art. 7 AVR' op een bord in ruimtes op NS-stations schept geen duidelijkheid over de bestemming en is derhalve zinloos.

13. Het hanteren van een uniforme pensioengerechtigde leeftijd is een miskenning van de individuele mogelijkheden en talenten van ouderen.

14. Doctores zijn ook mensen.

15. ...'De dominee, de dokter, de notaris,
Drievuldig beeld van al wat wijs en waar is.
Maar 't kan verkeren'... (J. Greshoff)

Stellingen behorend bij het proefschrift van François Schellevis: Chronic diseases in general practice. Nijmegen: Katholieke Universiteit, 30 november 1993.